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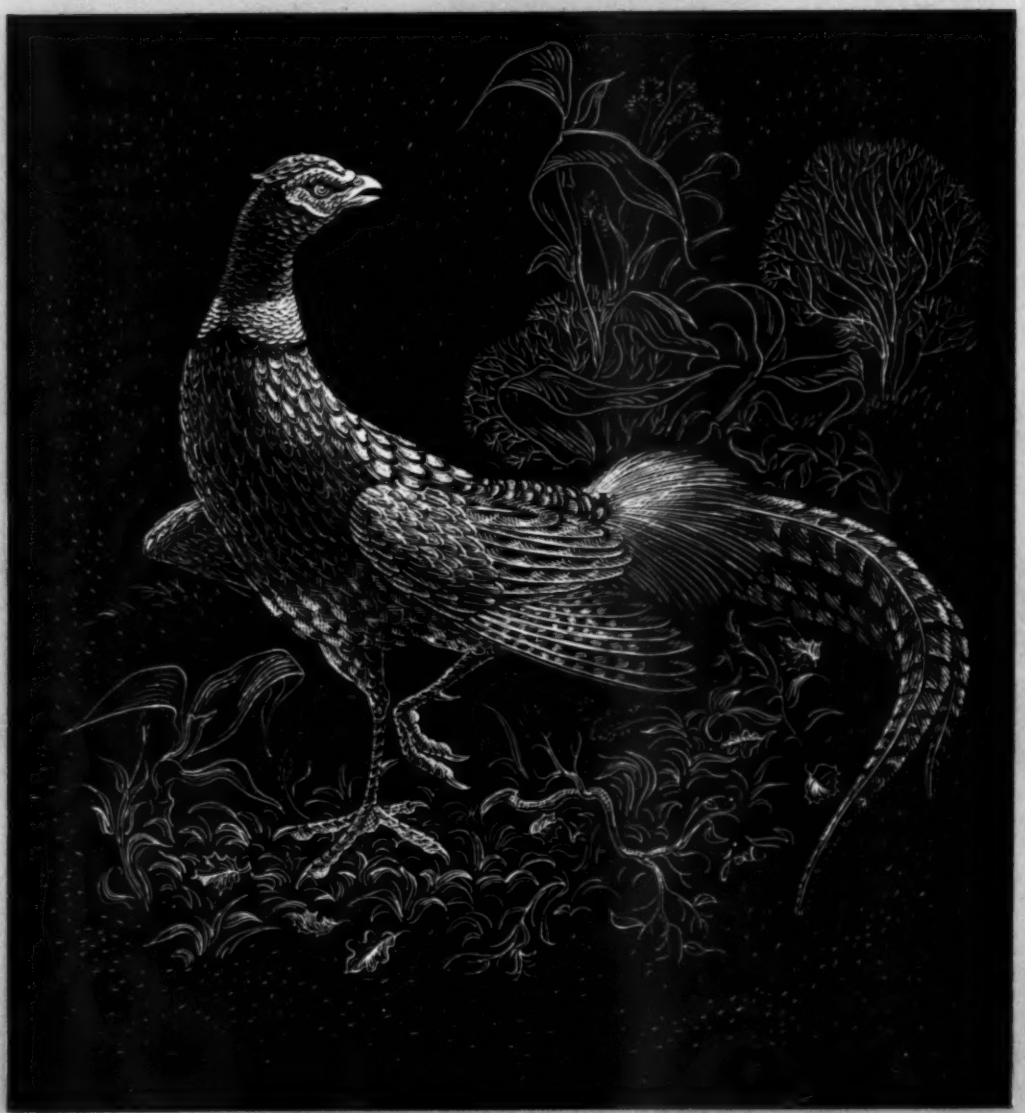
Drug and Cosmetic Industry



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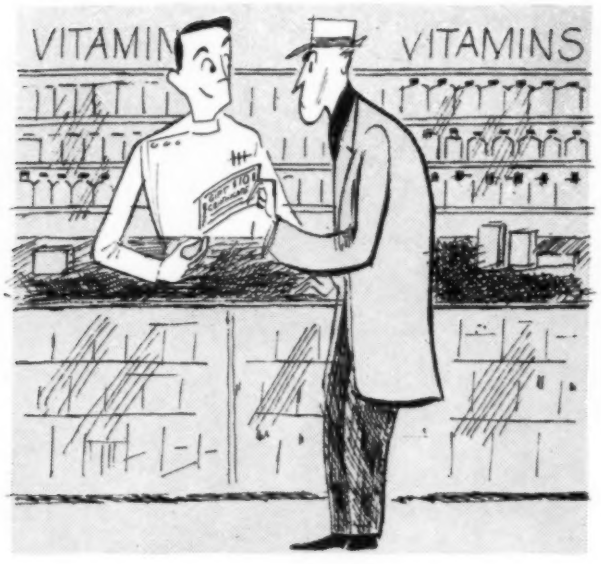

"How many capsules can I get for this gift certificate?"

Keeping Posted

Ten Years of Fluoridation

The year 1955 marked the completion of ten-year tests of fluoridation in three North American cities—Grand Rapids, Michigan; Newburgh, New York; and Brantford, Ontario. Overall rates for the three cities showed a reduction of nearly 60 per cent in dental decay when compared with pre-fluoridation experience, according to Dr. H. Trendley Dean, secretary of the Council on Dental Research of the American Dental Association. "The results from these three cities evidence the gradual transition of the theory of fluoridation into a scientific law," he said. Dr. Dean said that an increasing number of reports from numerous other independent studies "merely augment the overwhelming mass of scientific evidence" on the measure's effectiveness, safety, and economy.

Fluoridation was described as "the most promising factor" in resistance of the teeth to decay by Dr. David F. Mitchell, of Indianapolis, professor and chairman of the department of oral diagnosis, School of Dentistry, Indiana University. Dr. Mitchell said that while many theories have been advanced on the causes of dental decay, the most important proved factors are the inter-action of sugars and acid-producing mouth bacteria. Saying that most of the public's dental bill of an estimated one and one-half billion dollars a year is the result of the ravages of tooth decay, he observed: "It is estimated that the current rate of dental decay is six times as great as the rate of dental repair."

That decades of research indicate that "a positive relationship" exists between the amount of sugar in the diet and the extent of dental decay activity in persons, is the opinion of Dr. Philip Jay, of Ann Arbor, professor of dentistry at the School of Dentistry, University of Michigan, and Alice Bennett, instructor in dentistry at the school. "These findings have stimulated a great deal of controversy during the last 30 years but they have withstood the test of time very well," they said. They also noted "the remarkable effect" of fluorides on dental decay.

"It has been demonstrated conclusively that the use of domestic water containing one part per million fluoride will reduce the prevalence of caries greatly if the water is used during the first eight years of life," they said.

Frates—Drug Man of 1955

George H. Frates, Washington representative of the National Association of Retail Druggists, has been elected as the retail drug field's Man Of The Year 1955, according to the American Druggist which created the award to honor the man who makes the most constructive contribution to the welfare of the retail drug field during the year. The selection is made by a panel of drug industry leaders, including the presidents and secretaries of all national, state, and local pharmaceutical associations, the deans of all accredited colleges of pharmacy, and the editors of all national, state, and sectional drug publications.

Mr. Frates was honored because of two accomplishments in 1955: He guided the drug campaign which resulted in the issuance this year by the U.S. Narcotics Bureau of a list of narcotic products approved for dispensing on oral prescription. He also helped to rally opposition to the anti-fair trade and anti-Robinson-Patman recommendations of the U.S. Attorney-General's antitrust law committee.

Thirty-one different nominations, of which five were far in the lead, were made for the award. In addition to Mr. Frates these included:

Robert A. Hardt, vice-president of Hoffmann-La Roche and chairman of the public relations committee of the American Pharmaceutical Manufacturers Association. Mr. Hardt organized the Rensselaer Polytechnic Institute program through which hundreds of high school teachers learned of Pharmacy's services to the public welfare.

Jennings Murphy, secretary of the Wisconsin Pharmaceutical Association, who directed the newspaper campaign whereby the druggists of Wisconsin sought to educate the public on dangers involved in obtaining medication from untrained unlicensed assistants in doctors' offices.

Joseph H. Stamler and Murray F. Cleveland, two attorneys who as a team successfully overcame the attempt of Schwegmann supermarkets of New Orleans

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to obtain a fair trade court ruling that fair trade cannot be applied to prescription products.

FDA Barbiturate Legislation

The Food and Drug Administration has drafted legislation for the control of illicit traffic in barbiturates and amphetamines to be introduced in the current session of Congress. The bill is based on illegal possession of these drugs and would permit seizures to be made on this basis. Also the principle of the oleomargarine amendment to the Food, Drug, and Cosmetic Act, whereby colored oleomargarine is declared to be a product of interstate commerce regardless of the fact that it may never enter interstate commerce and may be sold entirely within the state of manufacture, will be applied to barbiturates and amphetamines. The bill makes possession of barbiturates and amphetamines a federal offense unless the drugs are obtained on prescription or unless the drugs are in the possession of a person regularly and lawfully engaged in the manufacture or distribution of drugs.

Another feature of the bill, and one that might meet with opposition from some parts of the drug industry, is a requirement that any company dealing in the drugs keep records of production, shipments, and receipts, and make such records available to FDA inspectors.

Armour ACTH Patents Upheld

Armour ACTH patents have been upheld by the Federal District Court in California and a consent decree has been entered against Pacific Laboratories of Richmond, California. The patents upheld, Nos. 2,669,536 and 2,669,537, cover ACTH products and methods of manufacturing. Pacific Laboratories was restrained from infringing the patents in manufacturing or selling ACTH.

Drug Store Sales up Six Per Cent

Sales by U.S. drug stores during 1955 were 6.3 per cent greater than in 1954, and total drug store business amounted to an all-time record of $4,810,000,000, according to an estimate by Dan Rennick, editor of the American Druggist. The estimate covers sales only by bonafide drug stores—that is, stores which maintain prescription departments. It is estimated that about 25 per cent of the sales were accounted for by prescriptions alone, which totaled in number approximately 465,000,000. It is forecast that 1956 will bring about a five per cent increase in prescriptions, largely because of new drugs which will be made available.

As a result of the increasing importance of drugs and prescriptions in the retail drug field today, many new drug stores built during 1956 will have the prescription department located up front instead of in its traditional location in the rear of the store, it is forecast. Fully 20 per cent of the nation's drug stores now operate on a self-service basis, except for prescription, drug, and fountain departments. Only four years ago, fewer than two per cent of all drug stores provided self-service.

Dow Sees More Expansion

A whole new round of industrial expansion may be started in 1956, according to the view expressed by the management of The Dow Chemical Company in taking its annual year-end look at the past and the future. It is pointed out that, beginning in 1950, American industry built capacity with the objective of providing both "guns and butter." It turned out that most of the production went for peaceful purposes, and those peaceful purposes are now absorbing just about all industry can produce.

Steel, chemicals, synthetic rubber, aluminum, and glass are cited as examples of basic industries that have "just about used up their capacities" and must look to major expansion. The Dow people think this will be felt some in 1956 but even more in 1957 because of the inherent lag between planning and construction.

The coming year will be an even better year for business than was 1955, according to Dow executives. But it might follow a somewhat different pattern. They note that 1955 started slow and economy gained speed as the year progressed. Indications are that 1956 will get off to a vigorous start but, Dow thinks, could decelerate before the year end. They do not foresee a downturn in the economic curve but rather the possibility of some flattening.

Dow itself spent about $50 million for construction in 1955 and expects to spend at least $75 million in 1956. Among new plants brought into operation were facilities for production of glycerine, polyethylene, and soda ash—all new products for Dow. The company also expanded its capacity for ethylene glycol, polystyrene, Styrofoam, saran and saran film, and added to its laboratory facilities.

Federal Medical Research Expansion

An expansion of the medical research programs of the federal government by as much as 25 to 30 per cent in funds for the next fiscal year will be asked of Congress by the administration, according to Secretary of Health, Education, and Welfare Marion B. Folsom. Total appropriations for the current year for the National Institutes of Health were $397,800,000. The broad outlines of the expansion program are:

Increased funds for each of the seven major categories —mental health, cancer, heart, arthritis, neurological, dental, and microbiological. Recommendations from advisory councils in each specific field are being coordinated into a balanced overall program.

More emphasis on basic medical research—fundamental studies in biology, biochemistry, physiology, pharmacology, and other sciences which may open new frontiers against many diseases.

Research operations at the National Institutes of Health to be expanded, but most of the additional funds to be allocated in grants for research projects by others—medical schools, hospitals, health agencies, private laboratories, and individual scientists — throughout the country.

Funds for fellowships to develop more research scientists would be increased substantially.

Secretary Folsom points out that for these increased

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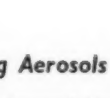

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funds to achieve maximum effectiveness, further action is necessary to relieve the shortage of scientists and of research facilities. In providing funds for medical research, it would be wise to help provide the men and facilities to use the funds soundly. For this reason, he said:

"This administration will recommend to Congress a new program of federal assistance to medical and dental schools and non-profit research institutions for the construction of research, training, and teaching facilities. Federal grants would be administered by the Public Health Service and would be matched by the institutions. The combined funds would help materially in meeting the need for more research facilities and for training more physicians, dentists and scientists for medical research. Funds would be allocated throughout the nation on the basis of the most worthy applications received from institutions."

Cancer Facts

The largest cancer survey ever conducted in any country was completed last month in 10 American metropolitan areas by the National Cancer Institute. Cancer incidence, prevalence, and mortality rates were surveyed in 1937-39 and 1947-48 in Chicago, Detroit, Philadelphia, Pittsburgh, Atlanta, New Orleans, Dallas, Denver, San Francisco, and Birmingham, Alabama. The survey was on "a scale unrivaled in any other country" and could not have been undertaken without the support of state and county medical societies, it is reported.

The survey showed that in 1947, 430 of every 100,000 residents had cancer at some time during the year—26 per cent more than in 1937, and 149 of every 100,000 died of cancer—an increase of 19 per cent in 1947, 319 new cases were diagnosed for every 100,000 persons—30 per cent more than in 1937.

The survey also revealed that:

Thirty-two of every 100 newborn children may expect to develop cancer at some time during their lives, if present rates continue.

Of those 32, three may be expected to develop cancer by age 45, 14 by age 65, 23 by age 75, and the remainder in after years.

More than 500,000 new cases are being diagnosed in the United States each year. At current rates, cases may be expected to increase by more than 50 per cent in the next 25 years, since both total population and the proportion of older people are expected to increase. Cancer illness rates increase rapidly during adult life and old age—at rates of about 40 per 100,000 at age 25; 475 per 100,000 at age 50; and 1,900 per 100,000 at age 75.

Adjusting for age difference, cancer is discovered at the same rate among men and women (331 and 330 per 100,000).

The death rate is higher for men than women (169 against 147 per 100,000). This is due mainly to the fact that cancer in men originates more frequently in such sites as the stomach and lungs, with poor chances for recovery.

In men the risk of cancer of the digestive system is dominant, with a lifetime probability of 10.3 per 100.

In women the risk of cancer before 65 is highest in the reproductive organs—a rate of 7.2 for the genital organs and 7.5 for the breast per 100. After 65, the risk is greatest in the digestive system.

Nearly all forms, except cancer of the reproductive organs, occur more frequently among men.

Cancer of the lung and bronchus occurs four and one-half times more among men than women. The laryngeal cancer rate is 12 times greater.

Incidence and mortality for cancer of the lung more than doubled from 1937 to 1947. This may be due partially to improved case finding, but part of the rise is real.

In 1947 cancer was diagnosed at a rate of 272 per 100,000 among nonwhite persons, compared to a rate of 333 for whites. Skin cancer is relatively rare among nonwhites, while among white persons the skin accounts for one in seven cancers. The low nonwhite rate is generally considered to result from "a true racial difference in susceptibility."

From 1937 to 1947 the number of cancer patients seen in hospitals increased seven per cent—from 68 to 73 per 100 patients.

Awards for Medicine and Pharmacy

The annual awards for distinguished service to medicine and pharmacy of the Alumni Association of the St. Louis College of Pharmacy and Allied Sciences are to be conferred on February 26. The 1955 award for service to medicine will go to Dr. Evarts H. Graham, professor emeritus of Surgery, Washington University School of Medicine, known throughout the world for his pioneer work in the field of thoracic surgery, and more recently for his studies of the relationship of tobacco smoking and lung cancer.

The 1955 awards for service to pharmacy will go to: Orval J. Cloughly, president of the St. Louis Wholesale Drug Co.; Fred W. Nehring, professional service manager of E. R. Squibb & Sons; Herman W. Reuter, honorary president of the Retail Druggists Association of St. Louis; Arthur F. Schlichting, Ph.D., dean of St. Louis College of Pharmacy and Allied Sciences; Oliver J. Steppig, past president of the Missouri State Board of Pharmacy and chief pharmacist of Alexian Brothers Hospital; and Leroy A. Weidle Jr. president-elect of the American College of Apothecaries and vice - president of the Knight Drug Company.

National Pharmaceutical Council

All segments of the pharmaceutical industry have indicated their acceptance of the objectives of the National Pharmaceutical Council in strengthening ethical standards and thereby gaining public goodwill, Dr. Theodore G. Klumpp, president of Winthrop Laboratories, told a gathering of 100 industry leaders at a luncheon given in his honor upon his retirement as president of the NPC. "Indeed, the drug industry has signified there is a vital need that these objectives be realized," said Dr. Klumpp.

In introducing his successor as president of NPC, Robert A. Hardt, vice-president of Hoffmann-La

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The outstanding individual performances of BACITRACIN, NEOMYCIN and TYROTHRICIN are enhanced by their combined use as a team. These three antibiotics, manufactured by S. B. Penick & Company, offer a broad attack on bacterial organisms invading skin surfaces, oral and pharyngeal tissues, and against gastro-intestinal dysenteries.

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Roche, Dr. Klumpp—as an indication that his successor would be busy at his new job—presented him with a gold-plated key to the men's room at Radio City where the offices of NPC are located.

Mr. Hardt then made a presentation on behalf of the NPC of a silver service to Dr. Klumpp and Mrs. Klumpp who was also present at the luncheon.

Membership of the NPC now stands at twenty pharmaceutical manufacturing companies.

Lueders Not For Sale

We are informed by George Lueders & Co., New York essential oil house established seventy years ago, that the company is not for sale. A statement from the company reads:

"This rumor has again become persistent and the president of the company emphatically denies any such intention. As a matter of fact, the company claims business continues to be very good, thanks to their many loyal friends and customers."

Hugo Schaefer Heads Conference

Dr. Hugo E. Schaefer, dean of the Brooklyn College of Pharmacy, who is retiring from that position in the near future, was elected president of the National Drug Trade Conference last month. Harold C. Kinner, of the National Association of the Boards of Pharmacy, who was reelected vice-president of the Council, was a member of the nominating committee and insisted that Dr. Schaeffer be the nominee when the committee was in agreement that Mr. Kinner himself should be advanced. Ray C. Schlotterer, of the Federal Wholesale Druggists Association, was reelected secretary-treasurer.

The Conference went on record as of the opinion that any further legislation dealing with hypnotic drugs be left to state rather than federal authority. The group also expressed the belief that sale of Salk vaccine should be through regular distribution channels, and should be distributed on a free basis only to the indigent.

Much interest was displayed by delegates to the conference on the subject of instituting a central public relations program in the drug industry. The Conference adopted a resolution urging that if a public relations program is undertaken, all segments of the drug industry should participate in it.

Pain-Killer Claims

Wernet Dental Manufacturing Co., Inc., trading as Hudson Products, Jersey City, has been charged by the Federal Trade Commission with falsely advertising Sentrol as an "amazing new capsule"—"three times more effective than aspirin." The product, according to the FTC, is nothing more than a particular combination of ingredients known to the medical profession for many years. The "pain-dulling" effect, says the FTC, is no greater than aspirin, both products are capable of temporarily relieving mild headaches but not severe ones. The salicylamide in Sentrol is neither the most amazing discovery nor one of the most effective pain relievers yet discovered in modern medicine, according to the complaint. In addition, contrary to the firm's claims, the complaint charges that Sentrol can cause stomach upset and will not relieve headaches which aspirin can't help.

Eye-Lash Claims Stopped

A consent order issued by the Federal Trade Commission prohibits advertising claims that Talika Eye Lash Creme, a product of Natone Co., Los Angeles, will grow longer or thicker eyelashes.

Pfizer Stops Squibb in Cuba

Chas. Pfizer & Co. recently obtained an injunction in a Cuban court prohibiting the E. R. Squibb Inter-American Corporation from selling, distributing, or using tetracycline. This decision was the result of an action for patent infringement instituted by Pfizer last September, which followed soon after the grant to Pfizer of basic patent protection on tetracycline in Cuba. Pfizer has two patents in Cuba on tetracycline, one covering production of the drug by direct fermentation, and the other covering the manufacture, use or sale of tetracycline regardless of the method of production or type of formulation.

Restrictive Sales at Conference

The restrictive sales problem was one of the major topics discussed at the Drug Trade Conference last month. Read at the Conference in opening the subject, was the report of a special subcommittee composed of A.Ph.A. Secretary Robert Fishelis and Proprietary Association General Counsel James F. Hoge, which subcommittee had been appointed by the Conference Committee on State Legislation. The subcommittee report had been accepted by, and offered as the report of the full committee.

This report sought to face up to the facts in the restrictive sales problem by stating the areas of agreement and disagreement between retail pharmacy on the one hand and proprietary manufacturers on the other. The report concluded that "the solution of the problem requires a specification of the kind of packaged drugs and medicines which may be sold in retail outlets other than pharmacies." The report then indicates two separate ways in which this can be accomplished:

1) The formulation of a definition of the usual phrase "patent and proprietary," or 2) The description of the class of exempt articles without use of any phrase or name to identify them.

Stating that "both methods have been followed in state pharmacy acts of recent years," the report says: "It is very likely that the existing controversy has been intensified and sometimes beclouded by overemphasis upon the term 'patent or proprietary medicine.' Courts have been disinclined to give it a precise definition and have indicated that it must be applied product by product, in ever recurring litigation. If this is so, then the solution may be aided by doing

away with the term, or at least lessening the concern for it, and putting the full weight of consideration on the realistic factors which should be determinative of an article's exemption from the basic restriction. The Committee recommends that further effort to resolve the controversy move in that direction."

Will Not Grow Hair

The Wybrant System will not grow hair "in a majority of cases," even with its triple shampoo, double application of "scalp tingling" lotion, steam treatments and massage, it is charged bythe Federal Trade Commission in a complaint brought against Wybrant System Products Corp., New York. Neither will the system permanently eliminate dandruff or itching scalp, the Commission alleges. In truth, the complaint maintains, the system will not prevent the common types baldness of hair loss or grow hair when its loss so originates. "The great majority of cases," the complaint states, stem from this common type baldness, which originates in heredity, endocrine balance, and aging.

Analysis of the various Wybrant preparations by the Commission reveals that of the two shampoos used in the system, one is the regular coconut oil base shampoo, and the other is a detergent type shampoo which is diluted in four degrees depending on hair type and is designated Shampoo 5 through 8.

Lotion No. 2, or the Wybrant formula, claimed by the firm to be largely responsible for its success in treating hair, the complaint states, is 97 to 98 per cent water and three per cent oil of wintergreen, gum, perfume and/or other oils, "a trace of a light hydrocarbon," and "a sulfated or sulfonated surface active agent." Lotion No. 4, according to the complaint, is a perfumed toilet water or hair dressing. The oil used is a light mineral oil designated No. 3 plus an oil paste.

Vitamin and Hematinic Sales

With the possible exception of the antibiotic-vitamin combinations, total sales of vitamins and hematinics on prescription for 1954 is estimated at $43 million, according to Modern medicine, while sales made in drug and other stores over the counter and by house-to-house direct to consumers account for another $62 million, while figures on sales to physicians, hospitals, and institutions for administration and dispensing are just not available, and any guess could very well be wide of the mark.

Vitamin and hematinic prescriptions for 1954 are estimated at 12,795,300, valued at $19,396,111. These prescriptions represent 42.5 per cent of the total vitamin prescriptions for 1954 of 3,101,128, and their value represents 45.3 per cent of the total value of $42,726,521. Other major classifications are multiple vitamins, 4,486,156 prescriptions (14.9 per cent), valued at $7,477,748 (17.5 per cent; vitamins and minerals, 2,661,964 prescriptions (8.8 per cent), valued at $4,437,069 (10.4 per cent); B complex, 1,630,216 (5.4 per cent), valued at $2,080,156 (4.9 per cent); dietary supplements, 1,424,408 prescriptions (4.7 per cent), valued at $2,319,740 (5.4 per cent); vitamin B_1 and combinations, 1,102,156 prescriptions (3.7 per cent), valued at $1,110,106 (2.6 per cent); calcium-vitamin D combinations, 972,172 prescriptions (3.2 per cent), valued at $746,528 (1.7 per cent); vitamin B and combinations, 939,676 prescriptions (3.1 per cent), valued at 538,136 (1.3 per cent).

Pfizer Licensed on Prednisone

Schering Corporation recently concluded a patent licensing agreement with Chas. Pfizer & Co., covering the manufacture and sale of prednisone and prednisolone. Schering markets prednisone under the trademark name Meticorten, and prednisolone as Meticortelone. Pfizer's brand of prednisone is marketed as Sterane. Schering President Francis C. Brown points out that all U. S. manufacturers of these products have now entered into license agreements with Schering.

Bristol-Myers Pension Changes

Bristol-Myers Company made major changes in their pension plan effective January 1. Employees' contributions will continue to purchase group annuities, exclusively, as heretofore. The company's contributions, however, approximately double those of the employees, will be invested in a common stock fund to be known as the Bristol-Myers Retirement Fund. Some of the company's contributions, when necessary, will be used to purchase annuities. Philip C. Sayres, executive vice-president of the company and chairman of the newly-formed Pension Committee, announced additional changes which include a lowering of the "vesting right" from fifteen years to ten years, and the creation of a death benefit for employees' beneficiaries from the Retirement Fund.

"The revision of the pension plan," said Mr. Sayres, "should go a long way toward taking up the slack caused by inflation. It is the intention of the Pension Committee to make regular purchases of securities each month upon advice of investment counsel. The committee will not attempt to guess the market, but will consistently purchase high grade equities."

Federal F., D., and C. Laws Committee

Adam H. Fiske, Eli Lilly and Company, has accepted the chairmanship of the Drug, Chemical, and Cosmetic Industries Committee for the 50th Anniversary of the Federal Pure Food Law which will be observed nationally this year. The committee, appointed by Eugene H. Holman, president of Association of Food and Drug Officials of the United States, and superintendent of the Division of Food and Drugs of the Tennessee Department of Agriculture, has appointed a committee of 28 members representing all branches of this industry, including pharmaceutical, proprietary drug, cosmetic, and chemical manufacturing; all branches of drug retailing and wholesaling; and pharmacy and medical professional associations. The office of the Anniversary is located at 1145 19th Street, N.W., Room 505, Washington, D.C.

The Industry and the INVESTOR

"The drug business in the United States has had an outstanding record of growth in the last decade," says an industry survey of the drug business by Standard & Poor's, financial analysts. "Apart from a temporary downward deviation in 1952, sales have been a strong upward trend; the 1955 total is estimated at an all-time record of $1.6 billion," continues the report. Other facts and views given in this report published last month, are:

Sales of the ethical drug industry grew from $149 million in 1939 to over $1 billion in 1954, and research has accelerated to the point where a major new discovery each year is regarded as normal. At least 50 per cent of the indicated gain of $110 million in ethical sales in 1955 resulted from drugs introduced after April, 1954. One authority estimates that fewer than 10 per cent of the prescriptions now written by doctors could have been filled in 1935. New products, then, account for a larger proportion of total sales of the ethical drug industry than in almost any other business. Antibiotics, unknown prior to World War II, are today the largest single product category, accounting for approximately thirty-five cents of every prescription dollar.

The development of antibiotics points up the importance of research to the growth of the ethical drug business. As a majority of infectious diseases are now fairly well under control, research is concentrated on remedies for cancer, heart disease, virus diseases, mental disorders, and afflictions of the aged. Because of the satisfactory results obtained from broad-spectrum antibiotics, future emphasis in the antibiotic field is expected to be aimed at cures for specific classes of ailments.

With the growth of "miracle" drugs, the character of the drug business has changed. Mass markets invite competition. The field has been entered by many proprietary drug companies, chemical companies, and others, with the result that the industry has a minimum 20 to 25 per cent overcapacity in terms of current demand for antibiotics. Firms with earnings derived from one or two major new products have proved invulnerable to competiton from new entrants into the field as well as from European producers. Profit margins have declined as selling prices dropped, while expenditures for research and selling have necessarily been increased. Old-line ethical houses met the challenge in part by mergers or other forms of consolidations.

While the growth in proprietary drug sales has not been as spectacular as that in ethicals, expansion has been steadier and more orderly, averaging about four per cent in each of the last five years. Continued sales expansion depends to a large extent upon consumer advertising and merchandising. These sales are relatively insensitive to changes in consumer incomes, and tend to follow increases in the population. Demand for proprietary drugs is being stimulated by the aging of the population and by the tendency of the geriatric group (over 65) toward self-medication.

Research expenditures in the proprietary group have risen considerably, and some estimates now place the ratio of research costs to sales at one-third to one-half of the amount spent on ethicals.

Sales of cosmetics are directly affected by changes in consumer incomes. The industry has been able to maintain its 0.4 per cent share of the rising consumer disposable income by new product development and a broadening of the market to include men's cosmetics and new women's products. Additional factors that have aided the industry have been the increase in population, and shifts in population to urban and suburban areas, where more cosmetics are used than in farm areas.

Proprietary and cosmetic companies have more and more encroached on each others' preserves as well as the ethical field. Companies that have done this successfully have created a base for more stable and more profitable operations.

Foreign operations account for an important portion of the sales and profits of the entire U.S. drug industry. Despite the resurgence of European drug manufacturers and continuance of burdensome exchange restrictions, most American drug firms are still expanding their overseas business. In 1954, exports of drugs and medicinals totaled about 15 per cent of overall sales. This proportion is considerably understated because of the increasing number of

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Kenneth F. Valentine, president of the American Pharmaceutical Manufacturers' Association.

A. P. M. A. Meeting

Kenneth F. Valentine, president of the American Pharmaceutical Manufacturers' Association, who is also president of Pitman-Moore Co. of Indianapolis, Ind., addressed a press conference on the eve of the APMA's 1955 Combined Mid-Year and Eastern Section Meeting. The three-day gathering began on December 12.

"The research and development arms of the pharmaceutical industry are expanding their assault against the remaining major disease conditions on every front," Mr. Valentine declared.

Mr. Valentine noted that many APMA member companies were expanding research facilities—some at the cost of millions—to keep up with demands of their growing research programs.

"Research represents the very lifeline of the pharmaceutical industry.

"In our field we cannot simply change the color of a pill and expect to improve the nation's well being. We must maintain a high level of research. Much of

it takes us along very lonely paths where, frankly, we often do not know quite where we're headed. For every success of our researchers—for every sulfa, penicillin, prednisone, polio vaccine and tranquilizer—we can look back on thousands of failures," Mr. Valentine said.

"Yet we can also look around at literally millions of lives saved from death, from disability and distress," he said.

The APMA president stated that many research projects—particularly clinical tests—are financed by grants from pharmaceutical companies and conducted jointly with government agencies, non-profit health organizations and individual doctors.

"In addition we endeavor to bring such clinical information to the attention of the medical profession by supporting technical publications, sponsoring graduate symposia, exhibiting at medical conventions and awarding fellowships," Mr. Valentine said.

Dr. Ralph Bunche, Under Secretary of the United Nations, headed the list of 18 top representatives of government, business, education, medicine, journalism and the drug industry itself, who participated in the APMA meeting. They addressed members at three morning and two afternoon sessions, a special award dinner and a closing luncheon. Program chairman for the annual exchange of scientific and production information was Francis C. Brown, APMA eastern vice president and president of Schering Corporation of Bloomfield, N. J.

The entire December 13th afternoon session was devoted to the topic, "Drug Therapy in Mental Disease?" Three eminent psychiatrists discussed the significance of the new tranquilizing drugs.

At the special award dinner, Dr. Bunche introduced Dr. Charles William Mayo, who had been nominated to receive the APMA annual award for 1955. Internationally known as a medical writer and editor and as a surgeon at the renowned Mayo Clinic, Dr. Mayo was honored "for his significant and lasting contribution to medicine and world understanding," as a member of the U. S. delegation to the Eighth General Assembly of the United Nations.

Other day sessions of the meeting were devoted to a variety of subjects, including export problems, motivation, packaging, quality control, tablet making, economic trends and others. Speakers included Dr. Morris Fishbein; U. S. Senator Mike Monroney of Oklahoma; Kennerly Woody, vice president of the New York Telephone Co.; Alan H. Temple, executive vice president of the First National City Bank and William I. Nichols, editor-in-chief and publisher of This Week magazine. Drew Pearson, Washington columnist, addressed the closing luncheon Wednesday, December 14th.

The meeting, which was held at New York's Waldorf-Astoria, marks the 46th year of the APMA.

Some of the papers delivered before the association are given in abstract.

Dr. Morris Fishbein discussed the problem of **Uniform Procedures for Product Registration and Labelling in Latin America.** The extension to Latin America of pharmaceutical products has been hindered and delayed and impeded by a multiplicity of complex and intricate laws and regulations that baffle even the expert export managers of leading pharmaceutical industries throughout the world.

The difficulties in securing admission of new pharmaceutical products into Latin American countries include the excessive length of time necessary to obtain the approval of governmental officials for entrance of products into the country. The standards regulating labeling vary so greatly from country to country that it becomes exceedingly difficult for a manufacturer to distribute throughout all of Latin America. In many countries the material required for an application is so complicated as to discourage even an application. Moreover, the procedures concerned may have to pass through the hands of so many bureaucratic agencies with differences of opinion as to make it burdensome and costly to follow.

A resolution of the recent meeting of the Confederacion Medica Panamericana in Bogota in October directed the establishment of a committee to be concerned with the problem of registration of pharmaceutical products. It urged the formation of an inter-American convention for the purpose of drafting a code to make the recommendations of such committees effective. It also proposed a study of legislation in each of the countries by the member association of the Confederacion with a view to presentation to their governments of necessary modifications of such legislation in order to obtain the maximum uniformity of laws enacted in this respect in the various countries. Moreover, the resolution recommended that the basic standards previously developed by a study committee of the American pharmaceutical manufacturers be formed as the basis of a code of regulations to foundation in all the countries concerned.

Dr. C. W. Sondern discussed **The Economics of Raw Material Quality Control.** There is an increasing realization that the cost of quality control requires analysis. With the growing complexity of drug manufacture and laboratory testing procedures, costs may rise out of proportion to their value.

However, an inadequate program can be even more costly. The use of raw materials which vary from lot to lot in physical or chemical properties may lead to unacceptable pharmaceutical products.

Reevaluation of the effectiveness of sampling and testing procedures may reveal evidence that certain economies are feasible without reducing the safety factor of control operations.

The consequences of "rejections" were examined from both the buyer's and seller's viewpoints, and actual cost data taken from the quality control operations of a large diversified plant were reviewed.

Considerable interest was aroused by the discussion of **Tablet Press-Coating and Multilayer Compres-**

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FLAVOR ANALYSIS*

by Loren B. Sjostrom

Flavor testing programs in the pharmaceutical industry seem to fall into three general categories characterized by the type of tasters used: (1) random tasters (there is no semblance of panel organization), (2) informal panels, and (3) formal, trained panels.

The first category is the nearest to the old-fashioned method of asking anyone who happens to be handy what he thinks of a flavor. In this random type of testing, the person doing the flavor formulating may be somewhat selective by calling on people he feels have good flavor judgment. But ordinarily there is not a set number of people who taste, and formal records of responses are not made. This sort of testing is bound to be employed to some degree because of the convenience of asking the opinion of the man at your elbow, but does not take the place of a panel in supplying reliable information.

The informal panels go another step toward controlled flavor testing by having people assigned to do taste testing work as part of their job. They usually are people in the research department. Ordinarily the tasters examine a product at their leisure, rarely meeting together. However, responses are recorded and compiled, the composite serving as an interpretation sheet. The composites, incidentally, are usually distributed to the tasters for their interest.

Formal panels are yet another step toward scientific flavor development. Unlike other programs of flavor testing, panel members are not necessarily restricted to the research staff, but could include employees from other departments. Prospective panel members are screened by taste and odor tests that obtain an indication of the candidates' taste and smell acuity.

Formal panels used in the pharmaceutical industry are usually composed of 15-20 people who meet together to examine a product. In this way, there is an opportunity for exchange of ideas about the product's flavor—how well the unpleasant tastes are masked, if there have been any flavor changes, and what steps might be taken to improve the flavor. Results of formal panels are also carefully recorded; and often, when difference tests are used, the results may be analyzed statistically.

Of the four well-known pharmaceutical houses visited, the company that utilizes an organized flavor testing program has found the formal panels a great boon to the research and development program. The panel has been applied to several phases of the company's research and production: namely, in quality control, stability tests, and in each step of the formulation process. As has been found in other fields, the flavor panel serves in charting the course by providing definite information, which can then be interpreted and advantageously applied. To look at it another way, the panel might be compared to a compass, which provides information that is invaluable to a navigator. It is true that a navigator might reach port without a compass (and then again, he might not), but with the instrument he can get there faster and more economically. A panel serves in the same way.

Judging from the information accumulated on the tour of four pharmaceutical houses, no matter what type of flavor testing program is utilized, the trend is toward examinations that are not purely preferential. The various tests used are akin to assays in that they check the quality and effectiveness of a flavor.

Types of Tests

Tests that are commonly used are the paired-comparison, triangle, and ranking.

*Presented at the American Pharmaceutical Association, Philadelphia Branch on November 10, 1955, Philadelphia, Pa.

The paired comparison and triangle tests check differences. In the paired comparison test, the taster simply states whether or not he can detect a difference between two samples; whereas in the triangle test, the taster selects from three samples the one that is different. Perhaps these tests have found the most use in testing and screening prospective panel members, and also in checking raw materials. In the latter case, the objective would be merely to check if the incoming materials differ from the last batch. The difficulty with these tests is that no indication of degree of difference is obtained.

Ranking, on the other hand, in addition to determining whether or not differences exist, supplies information regarding the relation of samples to each other. Samples are arranged in order of increasing, or decreasing, intensity of a certain quality. In effect, the masking agent is ranked according to its covering value. This system is not feasible in working with bitterness—which is so often the problem in pharmaceuticals—because this quality builds up and is long lasting. Consequently, it is not practical to taste more than one sample in a short time.

There are, of course, variations of these tests. As in any research, the technique is tailored to suit the need. But for the most part these three tests seem to be the bases of the tests employed in the pharmaceutical industry.

Flavor Profile

Yet all these tests have the shortcoming of providing limited information in that they consider only one aspect of a product's flavor rather than the whole flavor. As flavor is assuming a more commanding role, it is necessary to look at the over-all picture in order to achieve and maintain a high-quality, appealing flavor. The flavor profile is a descriptive, semi-quantitative method that was originated at Arthur D. Little, Inc. to fill the need for a method that—unlike difference tests–could focus on the flavor in its entirety. The purpose of the profile is to project a reproducible analysis in which all the characteristics of a flavor can be considered in proper perspective. In a sense, it is a short cut to complete flavor information—information about not only differences, but also definition of differences, similarities, and likenesses.

The profile is a natural approach to analyzing a flavor and is actually very simple to use. The method is based on the concept that the sensation of flavor consists of a few recognizable characteristics (notes) protruding from a blended body of unidentifiable components. Briefly, four to six trained analysts individually "profile" a flavor according to (1) character notes of both aroma and flavor-by-mouth (including feeling sensations), (2) order of appearance of notes, (3) intensities of notes, and (4) total flavor effect.

The character notes are defined in descriptive or associative terms. For example, terms such as yeasty and sour might be used in describing the odor notes of thiamine. However, association with a definite chemical or other reference standard is attempted whenever possible. Sweet, sour, salty, and bitter are, of course, terms used for the basic taste factors. Feeling factors, such as cooling, bite, warming, and astringency, are often defined according to the location of the effect.

A simple, numerical scale is used for rating the intensity of the character notes: not present, just recognizable (threshold), slight, moderate, and strong. Finer distinctions can be made when necessary. This skeleton scale, which is surprisingly easy to use, is effective and adaptable.

After the panel members have individually analyzed the sample, an open discussion, moderated by the panel leader, is held to review the individual findings and to reach agreement in terminology used in defining the character notes. A profile is finally evolved when there is agreement regarding all aspects of the flavor, and a tabular record of the sensorial composition of flavor is drawn up—a record that can be interpreted for flavor correction and formulation. This profile gives direct information about the effects of the experimental treatment on the whole flavor of a product.

One of the major attributes of the flavor profile is its reproducibility. The same profile results can be obtained at separate times either by the same or different panels. Verification of this has been borne out in profile-panel training projects. At the end of such projects, trainee panels operating independently in their own plants consistently submit profiles corresponding to those obtained by the ADL panels. The 21 panels trained by ADL have all obtained profiles that agree.

Because the profile approach is so natural, in any system of flavor testing the tasters almost unconsciously describe and compare flavors, at least mentally, before making a decision. Even the wine taster profiles in a way. He looks at the whole flavor and evaluates its separate characteristics in relation to each other. It was interesting to note an assignment given to a panel member at one pharmaceutical house that uses an informal panel. He had been given a sample to examine with the instructions, "Describe the sequence of taste sensations." Essentially the instructions said, "Profile this sample." The taster said that he felt inadequate to do this. However, if he were trained in the profile method and could discuss his results in an open panel, he could cultivate the necessary competence and confidence to complete the assignment with relative ease.

Application of Profile to Drug Industry

This type of approach—the profile approach—would fill a niche in the pharmaceutical industry. It is another step away from hit-or-miss flavoring—a step toward providing sound information on which to

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T.G.A. Scientific

Dan Dahle, chairman of Scientific Section, Toilet Goods Association

Seven papers covering varied aspects of cosmetic science and technology were presented before Winter meeting of the Scientific Section of the Toilet Goods Association at the Waldorf-Astoria Hotel, New York, on December 14. Dan Dahle, with Harold D. Goulden, scientific director of the T.G.A., acting as secretary. The meeting was particularly well attended and interest in the papers presented was high. Abstracts of the papers follow:

Aerosol Spray Patterns were discussed in a paper presented by *M. J. Root.* The property that makes aerosol products unique as well as useful is the fact that they are self-propelled. By merely a flick of the finger a spray can be obtained. This spray can be characterized by the droplet size distribution, its area of coverage, its temperature, its wetness and liquid volume. The droplet size distribution is determined by the characteristics of the valve and button, the amount and type of propellent, the temperature and the viscosity and surface tension of the product. The area of coverage is defined by the angle projected by the spray and is dependent upon the design of the button. The temperature of the spray is determined by the amount and type of propellent used. Wetness of the spray is determined by the relative proportions of concentrate and propellent as well as the type of propellent which is used. The liquid volume delivered per unit time is a function of the valve inner orifices.

Various techniques have been developed for measuring these characteristics. The liquid volume of the spray is perhaps the easiest to determine since it merely involves spraying for a period of time and determining the amount of material dispensed. The measurement of droplet size distribution has received the most attention. A new dye technique has proven to be a valuable qualitative measurement of droplet size distribution as well as area of coverage. Spray temperatures have been measured accurately by means of a Thermistor instrument. The characteristics that are desired depend largely on the product and how it is used. It is possible to vary the spray characteristics by modifications in the formula, choice and amount of the propellent and selection of the valve and button.

R. L. Patterson delivered a paper discussing factors affecting the consistency of **Cream Shampoo Formulations.** Paste cream shampoo of the sodium alkyl sulfate, sodium stearate system consists of crystals in an aqueous liquor. The size, shape and mode of aggregation of the crystals is responsible for consistency variations in the shampoo during normal shelf life. If shampoo is chilled soon after packing, crystal growth is too rapid and results in a thin, glossy paste of fine short crystals. In very hot weather, too slow crystal growth can occur and this leads to a soft curdly product. At a controlled intermediate rate, crystals are formed which are sufficiently long and entangled to produce a mat which is strong enough to support its own weight.

Processing techniques which have pronounced effects on crystal growth include cooling time, end or packing temperature, and tempering or early storage temperature. These were discussed as well as the effects of some of the constituents in the formulation such as sodium stearate, free stearic acid, sodium sulfate, lanolin, and perfume.

A thorough review of the literature according to *G. Barnett* and *D. H. Powers* in their paper on **Performance of Shampoos** clearly establishes the need for a new definition of a successful shampoo. It is stressed that some *cleansing* and *foaming* action is needed, but it is more important that the hair be left *soft, lustrous* and *manageable.* In studying these five

Section meeting

characteristics of a successful shampoo, a new Latherometer was developed, and soaps, detergents and all of the leading shampoos were tested for their foaming and lathering action, varying the hardness of the water, the concentration of the detergent or shampoo, and studying the effect of sebum, sweat, soil, oils and hair dressings. A successful shampoo must have a high volume foam, with good stability and produce a "wet" foam. The new Latherometer appears to give reliable and reproducible results and correlates end-use or consumer performance with laboratory evaluation.

F. Cornman delivered a paper **Tissue Culture Applications in Pharmacological Evaluations.** Tissue culture is available for a wide range of uses. It is no longer a sharply circumscribed technique, but can be used for week-long observation of a single cell or mass production of billions of cells of a pure strain.

First and foremost, tissue culture tells whether a substance can act on a particular cell or tissue, and reveals what the alterations are. The criteria of effect can be morphological or biochemical. Many isolated tissues retain specialized functions. Nerve will conduct impulses, heart will continue to beat, and glands will secrete. Some organs maintain their complete structure and even grow: embryonic bone, for example. Thus where the nature of an effect cannot be pinpointed in the intact animal, it can sometimes be identified by its effect on isolated tissues. The special value of tissue culture becomes more obvious where metabolites must be traced. Hard-to-get fractions can be adequately tested in tissue cultures requiring a total medium of only a fraction of a milliliter.

The economy of tissue culture applies to the tissues as well. This is particularly valuable where we need to know the effect on human tissue without creating a hazard to the human being. Bits of tissue left over from surgery or biopsy can serve very well for in vitro testing. Being sterile, the cultures can be used for repeated tests.

Thus, tissue culture provides a simple approach to problems not easily answered by other means. It should be kept in the foreground of our thinking about pharmacological evaluation.

Measurement of Perspiration Activity was the subject of a paper by *O. Jacobi and H. Heinrich.* There is still need for discussion of the practical aspects of measuring antiperspirant activities from the cosmetic standpoint.

A number of methods using different principles have been proposed and used, most of them by medical research workers. A description of each major method was given and evaluated for possible cosmetic use.

Harold D. Goulden, scientific director, Toilet Goods Association

The various factors which cause difficulties in perfect duplication of results were given under the heading of active ingredients, equipment and test objects.

Four experimental methods were studied in detail and the results indicate that qualitative results and trends can be established but that quantitative duplication of results can only be obtained by statistical analysis of many experiments.

C. L. Bechtold, E. A. Lawrence and *E. M. Owen* discussed an invitro test for the effectiveness of **Antibacterial Agents in Soap.** The development of deodorant soap compositions necessarily requires the routine testing of potential antibacterial agents. Many of these agents are ineffective in the alkaline medium of soap, and may be rejected quickly from further consideration by the use of a test described in this paper—the Pellet Halo Test, a modified agar plate technique using pellets of the deodorant soap composition. The next phase of testing is ordinarily an *in viro* test such as that developed by Price and Cade.

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The new pharmacologic attack in psychiatry*

by Howard D. Fabing, M.D., CINCINNATI, OHIO

At the outset it should be stated that the new pharmacologic attack in psychiatry is not really very new after all. The ancient Greek and Roman texts, and the herbals which began to appear in medieval times and continued to be written in this country until the last century, are filled with the praises of a host of roots, leaves, flowers and seeds which were said to relieve the mind of man when it was sick. Burton's "Anatomy of Melancholy," which Sir William Osler kept at his bedside, and which he regarded as one of the world's most scholarly books, is a vivid example of the physician's search for psychiatric drugs in the world of botany. Burton's advocacy of the hellebore, or buttercup, family in the treatment of melancholia was enthusiastic.

The bromides were introduced into therapeutics in 1857—perhaps the first generally accepted chemical agent in the treatment of disorders of the nervous system. They attained a great vogue until it was determined that they could cause more serious mental illness on occasion than they attempted to treat. The next step occurred shortly after the turn of the century. The story is told that the famous German chemist, Emil Fischer, "dreamed up" the formula for the barbiturates while he was dozing in a railway carriage on a holiday in Italy. He looked out the window and saw that he was in the station in Verona, and so he named the new compound veronal. From this came phenobarbital, which is still one of the very best drugs we have, and which few clinicians have been able to abandon, try as they may.

The practising physician has always been fascinated by the fact that drugs which act primarily on the central nervous system are often two-edged swords. They tranquilize and they sedate for the most part, which is satisfying, but they may excite and intoxicate, too, which is not so satisfying. This mystery has never been explained adequately. In our search for specificity of action of neurotropic drugs we encounter the uncomfortable fact that we are dealing with an organ which is lacking in specificity in its very nature —the human brain. This does not make the pharmacologists very happy.

Pharmacologists, as I know them, are people with very neat and orderly minds. They have been trained to hook an animal up to a kymograph and get some very nice squiggles on a piece of recording paper. Then they introduce a drug of some sort, and they then get a very prompt and clear-cut change in the squiggles, a thing which any fool can plainly see, as Li'l Abner would say. Unfortunately, this won't work with the brain in most cases, as it does with the heart, the gut, or the urinary bladder. In the new field of neuropharmacology, or psychopharmacology as some are wont to call it, a whole new set of tools are needed. Men like Evarts, Heath, Marrazzi and Himwich are finding interesting new micro-electrical methods for studying drug action in the brains of animals and man, to be sure, but much of the action of these new compounds is dependent on a close scrutiny of total behavior, and much of it requires the human as the experimental animal. Neuropharmacology is new pharmacology. It requires a fresh point of view and the willingness to keep ever on the alert for the chance observation which may open new doors to the uninhabited rooms of our house of ignorance.

This kind of fortuitous observation, or serendipity, occurred in 1943 and, in my opinion, touched off much of the new inquiry into drug effects on the brain. Hoffmann, working in the Sandoz Laboratories in Basle, Switzerland, sucked up something in his mouth from a pipette. He had been working with ergot extracts, and was making esters of one of its components, lysergic acid. In less than an hour he was muddled, confused and hallucinated. Frightened, he left the laboratory and got on his bicycle. He pedaled what seemed like 5,000 miles to his home which was

*Read at a meeting of the American Pharmaceutical Manufacturers' Ass'n., Hotel Waldorf-Astoria, New York City, December 13, 1955.

in reality a short distance away, but he had lost time and space perception. He called his doctor who managed to get him to gulp down all the milk in the house, but his psychotic state persisted until he fell into a fitful sleep late that night. Four days later he returned to his laboratory, looked over his notebooks and decided that he had swallowed the dextro-rotatory diethylamide of lysergic acid. Gingerly he measured out a very minute amount of the material and took another swallow. The psychosis returned, this time worse. He pedaled 10,000 miles home, and again drank all the milk in sight to no avail. Thus LSD-25 was born. Here was an experimental way of producing a psychosis which had very much the look and feel of schizophrenia. It takes about one-seven-hundred-millionth of a healthy young man's weight of this material to produce a model psychosis of five to ten hours.

The minuteness of the dose and the magic of its effects have been tested and retested all over the world. One would have to be a stick or a stone not to have his imagination completely captivated by the drama of an LSD psychosis. Hoffmann's observation has fired clinicians, chemists, enzymologists and pharmacologists into new activity everywhere. It has caused us to take a new look into old things. Experimentation with mescaline, which had languished for the most part since the days of Wier Mitchell, has now picked up again. I know of two laboratories which are making a major study of this compound and its possible derivatives. A new look at the ancient narcotic snuff of Hispaniola and South America, cohoba, has shown that it contains bufotenine, a substance first found in the skin of poisonous toads. No self-respecting medieval Italian poisoner would have left toad-skin out of his brew. Recently it has been determined that the hallucinogenic mushrooms also contain bufotenine, and that this substance was probably behind the tribal debauches, characterized by temporary madness, which were indulged in by people as diverse as the Koryaks of Siberia and the Aztecs of Mexico, and perhaps even the Vikings of the north countries. Just two months ago we got some murderers at the Ohio State Penitentiary to volunteer for intravenous injection of bufotenine, which was kindly supplied to us by the Research Department of the Upjohn Company, and we found that it produced a temporary psychosis reminiscent of mescaline and LSD.

The metabolites of adrenalin have also come under scrutiny of late, especially in the schizophrenia research program in Saskatchewan, Canada. A very tricky compound, adrenochrome, has been found by this group of investigators to produce temporary schizophrenia-like psychoses of as much as four days duration. A search through anthropologic lore reveals that other compounds, such as yohimbine, harmine, and ibogaine have been used by man to transport himself into ecstatic states of visionary experience, through the doors of perception to the land of other-worldliness, as Aldous Huxley puts it. Nobody will contend that these states are schizophrenia, but they are very much like it, and they can be studied under controlled experimental conditions. In all this one senses the beginnings of a new scientific approach in psychiatry.

One of the fascinating things about these hallucinogenic drugs is that they are indoles. Are all indoles hallucinogenic for man? Emphatically, no. They are very common compounds in nature, ranging from the indigo dyes to auxin, the plant growth hormone, to skatole, which gives manure its stink, to serotonin, a neurohumeral agent which is under intensive study these days. The list of indoles in biology is tremendous. They are all very reactive compounds, and seem capable of changing from one to the other easily.

This tantalizing thought arises: rather than a disease we worry and fret ourselves into, is schizophrenia perhaps a biochemical disease, a disease of

(*Continued on page 125*)

Society of Cosmetic

Left to right, new officers for 1956 of Society of Cosmetic Chemists: Robert A. Kramer, secretary; Gabriel Barnett, director; George G. Kolar, president; Savery F. Coneybear, director; and Walter A. Taylor, treasurer.

Sabbat J. Strianse, president-elect of Cosmetic Chemists.

The Society of Cosmetic Chemists celebrated its tenth anniversary in New York City on December 15, in conjunction with its Annual Technical Meeting and Medal Award Dinner. A dinner-dance featuring the anniversary motif climaxed the birthday observance, at which the Society's founders were honored.

Launched in 1945 with 12 charter members, the Society of Cosmetic Chemists now has a total membership of 450 and a program of activities and awards that is international in scope.

The organization was the idea of Maison G. de-Navarre, who assembled eleven other charter members into the group designated as the Society of Cosmetic Chemists. The other founders were Philip Adams, James Baker, Robert E. Casely, Emery A. Emerson, Emanual G. Gundlach, Stephen A. Karas, Emil G. Klarmann, Raymond E. Reed, Marcel J. Suter, Walter A. Taylor, and Cloyce L. Thomas.

Today, ten years after its founding, the Society is known to scientists the world over, and its membership rolls are drawn from all the principal countries of the world. The parent organization has local chapters in Chicago and New York. The Society of Cosmetic Chemists of Great Britain is associated with the national group here.

Chemists meeting

The Society's Medal Award, a feature each year of the December meeting, is a citation that is internationally recognized and sought. Awarded for the first time in 1949, the medal honors outstanding work in fields relating to the art and science of cosmetics.

Dr. Ernest Guenther, internationally-known perfumer and chemist, was the recipient of the Society of Cosmetic Chemists' Annual Medal Award for 1955.

Dr. Guenther entered the cosmetic field in 1921, and for the next three years worked as chemist and perfumer on various European assignments. He came to the United States in 1924, when he joined Fritzsche Brothers as chief research chemist.

In his extensive explorations into the science of fragrances, Dr. Guenther has visited virtually every essential oil-producing region in the world, being equally at home in field, factory and laboratory. His world-wide studies have resulted in the establishment of precise specifications and rigid standards of purity for essential oils, which are the basis for today's vast perfumery and cosmetic industries.

The year 1948 saw the publication of the first volume of Dr. Guenther's authoritative study titled "The Essential Oils," the sixth and final volume appearing in 1952, representing over 12 years of intensive creative effort and a life-time of research and exploration. Recognized as an outstanding achievement in its field, the series covers every phase of essential oils considered important by industry and science.

Dr. Ernest Guenther, left, eighth recipient of Annual Medal Award, receiving Society's plaque from President Kenneth L. Russell.

Doctor George G. Kolar is president of the Society of Cosmetic Chemists for 1956. Other officers are: president-elect, Sabbat J. Strianse; treasurer, Walter A. Taylor; and secretary, Robert A. Kramer. The directors for the forthcoming year are Gabriel Barnett and Savery F. Coneybear.

The following are abstracts of the papers read at the annual technical meeting on December 15, 1955:

A paper **The Emerging Cosmetic Chemistry** by *Paul G. I. Lauffer* represents an attempt to characterize cosmetic chemistry, in terms of the kinds of papers the Society has heard in the past, and in light of recent progress toward solution of some of our more important problems.

Selected topics of current interest to cosmetic chemists were treated as examples of the multitudinous branches of science and the varied disciplines which impinge upon cosmetic chemistry. Among the topics treated were:

Composition and function of tissues, Cellular function, Enzyme mechanisms, Protein structure and formation, Allergic phenomena, Structure and physiological activity, and Aging.

In each of these fields recent advances were cited to illustrate how general concepts and empirical data are being replaced by detailed knowledge of the chemical mechanisms involved.

New Silicones for the Cosmetic Industry by *C. C. Currie and R. C. Gergle* described the chemical nature and general properties of three new types of silicones. Special emphasis was placed on properties such as compatibility with a variety of materials, light absorption and water repellency.

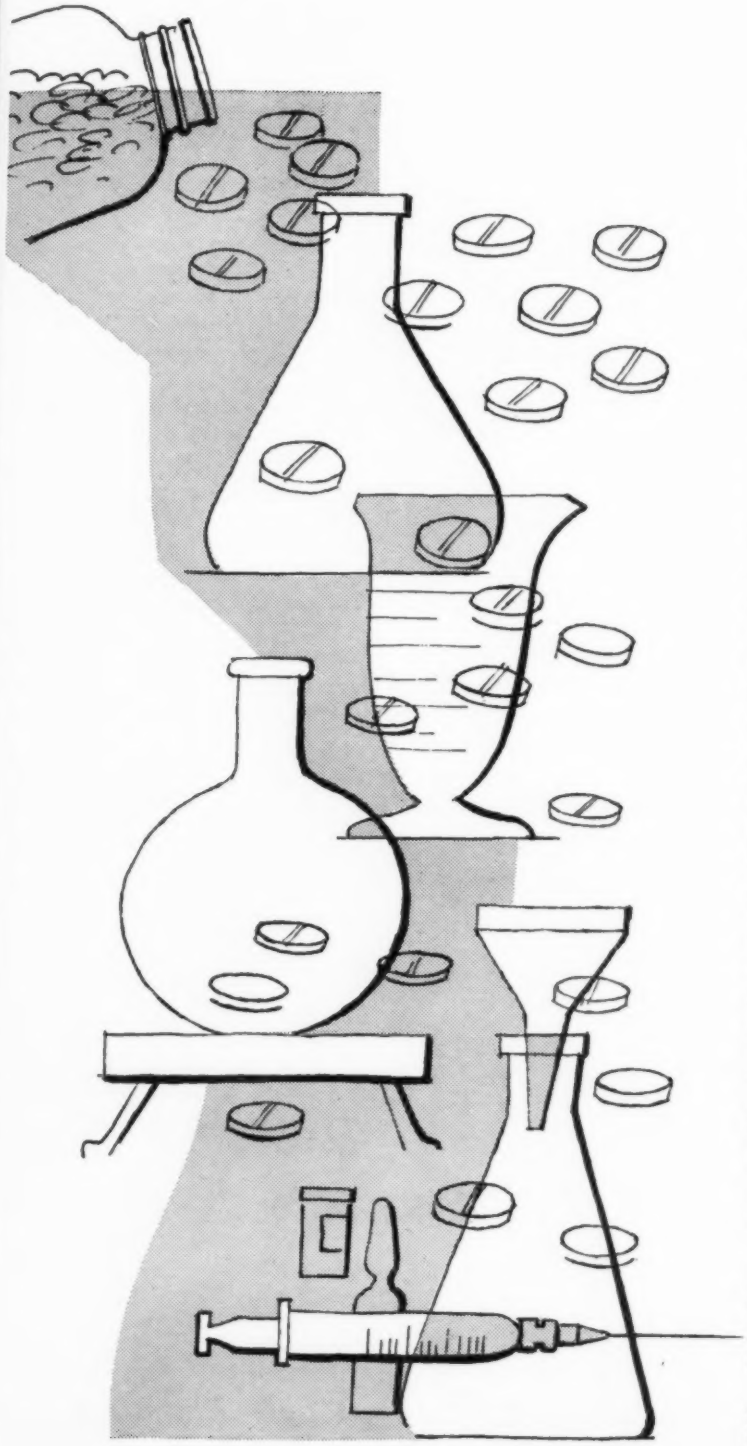
The first type of silicone is an hydrophobic silicone fluid exhibiting ultraviolet light absorption in the 220 to 420 millimicron range. This type of fluid may find use as a water repellent sunscreen agent. The second group of silicones consists of fatty alcohol esters of dimethylpolysiloxane. These wax-like silicones are generally soluble in waxes, esters and alcohols. They may be useful in lipstick and other solid cosmetic preparations. The third series of silicones are acid-free reaction products of ethylene glycol or polyethylene glycol with dichlorodimethylsilane. These liquid esters are soluble in many polar solvents.

A discussion, **Potential Utility of Ion Exchange Resins in Antiperspirant-Deodorant Formulations** by *J. C. Winters* described briefly the important physical and chemical properties of a group of ion exchange resins. With this information as background,

(*Continued on page 119*)

the PHARMACEUTICAL

by Dr. Theodore G. Klumpp, PRESIDENT, WINTHROP LABORATORIES



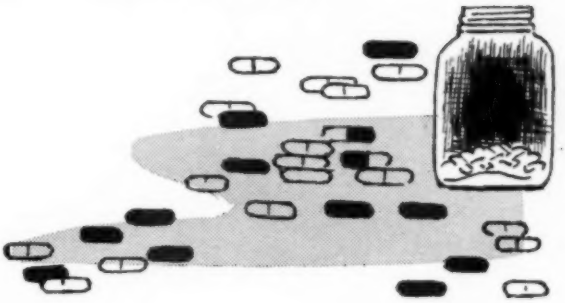
In the last fifty years more progress has been made in the conquest of disease and the prolongation of life than had been accomplished in the entire 999 centuries of man's previous existence on earth. The most eloquent summation of what has been accomplished can be expressed in terms of life expectancy which has moved upward from 49 years in 1900 to almost 69 in 1954. In 1900, among any average group of 1,000 persons, you could count on 17 dying that year. Today only nine of that same number will depart this world. Among infants the revolution is even more marked. At the turn of the century, of every 1,000 babies that survived birth, 162 died within the first year, whereas today less than 30 succumb. At the beginning of the twentieth century 7,000 children died every year of whooping cough. Last year only 310 died of this disease. Looking at it from another angle, we have seen the almost complete elimination of such killers as cholera, yellow fever, small pox and the plague. Diphtheria, scarlet fever, typhoid fever, typhus, tetanus, rickets, Rocky Mountain spotted fever, pernicious anemia, Addison's disease, meningitis and other diseases have lost their deadly sting. Tuberculosis was responsible for 194 deaths per 100,000 population in 1900, but only 10.6 in 1954. In half a century the greatest reaper of them all—pneumonia—has been all but defeated as witnessed by the fact that the death rate has declined from 152 per 100,000 to 12. Even among the survivors, at the beginning of the century, it took an average of three months' wages to pay the hospital bills resulting from a case of pneumonia. Today the disease is often cured at home at an average cost of only five hours' wages for the miracle drugs. Only forty years ago, one of every four persons subjected to a major operation met his doom, whereas today only one in a hundred succumbs, and if that still seems high, let us remember that surgeons can now operate where the risk is great, whereas a few years ago they would not have dared touch many cases that now have been given at least a fighting chance to live.

Forty-three years ago the existence of coronary thrombosis was not even recognized. Today it is diagnosed with certainty and measures are available to save the lives of many who would otherwise have succumbed.

The discovery of Insulin in 1922 is rightfully marked

*Before the Pharmaceutical Industry session of the Industrial Council, held at Rensselaer Polytechnic Institute, Troy, N.,Y., Oct. 27-29, 1955.

INDUSTRY and Health*



as one of the great milestones along the road of medical progress. The identification and extraction of a new medicinal principle are always events of great historical importance. But it is only the beginning and not the end of an achievement. A test tube miracle is one thing. Its beatification into thousands of gallons is sometimes a second miracle without which the first has no significance in terms of human betterment. And it is not until hundreds of thousands of small vials and ampuls or tablets pour out of some pharmaceutical plant, that the course of history is really influenced. Before Insulin two of every three diabetic patients died of diabetic coma. Today death from coma is so rare that a certificate with this diagnosis should attract the attention of the medical examiner.

On December 7, 1941, a shot was also heard around the world. More so perhaps than that first one on April 19, 1775, because this one meant that we were suddenly projected into a world war. And that shot woke up our military authorities and the experts in the newly discovered science of logistics, that we couldn't win that global war without a safe and effective antimalarial to replace the no longer available quinine. The American pharmaceutical industry supplied the need with close to seven billion tablets of Atabrine. Atabrine and its successor Aralen proved to be so good that quinine is now otherwise better occupied as an ingredient of another popular medicinal, gin and tonic.

Sir Alexander Fleming's penicillin was still only an almost unknown laboratory curiosity in the late thirties when the Oxford group led by Florey and Chain initiated their studies of it. By 1940 they had devised means of production and had treated a few patients. When called upon not long thereafter the enterprising American pharmaceutical industry willingly gambled millions of dollars that penicillin could be produced on a large scale and at a low enough cost for general use. Since penicillin, over four thousand antibiotics have been discovered in the United States, of which seventeen have been placed on the market. So far as I know, only one useful antibiotic has been developed in the rest of the world since penicillin.

It has been estimated that as many as nine million people, almost six per cent of the total population, are suffering from various forms of mental disturbance. Four out of every ten hospital beds in the U.S.A. are occupied with patients with mental illness. Our facilities are woefully inadequate and every mental institution has long waiting lists. From the standpoint of prevalence, this is now the most serious health problem in the nation.

Until recently the psychiatrist had almost no tools which which to work—very little more than talk and shock treatment. Talk in the form of psychoanalysis is too time consuming for general use and only applicable to a selected group of patients. Some are too dumb and others too smart for it. The other day a psychiatrist gave up on a brilliant young lady whom I happen to know. He said that she wound up by psychoanalyzing him. Shock therapy too has serious limitations.

But within the last two years our industry has come up with two drugs—Thorazine and Rauwolfia and its alkaloids—that have already revolutionized the treatment of some of the most prevalent forms of mental illness. In keeping with the history of our industry, when we once break through the sound barrier in a given direction, everyone seems to be able to do it and we have a flood of new and different products directed toward the same end. To digress a moment to illustrate the point, the first antihistamine was followed by hundreds of others, the first sulfa drug brought in its wake more than 5,000 others, the first antibiotic over 4,000 others, etc. A whole series of new compounds for mental illness have already been turned up and more are on the way. I am confident that we are standing on the threshold of a new and revolutionary era in the treatment of mental illness.

In the time available for this presentation it is only possible to refer to a few of the specific contributions of the pharmaceutical industry to health. I must leave unmentioned what we have done in the field of deficiency diseases, anesthetics, pernicious anemia and anemias in general, tuberculosis, high blood pressure, glandular products and a host of others. The whole story would fill a book.

I have no patience with those pigeon hole minds who are forever trying to compare the importance of things that can't be compared. Physics is more important than Chemistry, Chemistry is more impor-

(*Continued on page 121*)

Press-Coated and

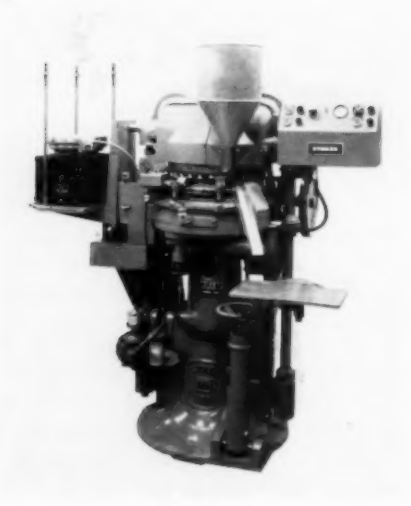


Illustration 1.
A tablet-within-a-tablet press with single rotary head and automatic hopper.

Illustration 2.
Loading core tablets into automatic hopper.

Illustration 3.
Properly press-coated tablets being ejected from machine.

Recently, two special tablet forms have excited many pharmaceutical manufacturers with their many possible applications. They are the press-coated tablet, or tablet-within-a-tablet, and the multi-layer tablet.

We will first consider the tablet-within-a-tablet: What it is, how it is made, and some of its typical applications. Then we will discuss several types of multi-layer tablets, how they are made, and their possibilities and uses.

Let us first define what a tablet-within-a-tablet is and what it looks like. A simple tablet-within-a-tablet, which is also frequently called a press-coated tablet or a dry-coated tablet, consists of a central core tablet made on any conventional tablet press and a press-coating, or outer tablet, made around this core tablet by the press-coating machinery that will be more fully discussed later. The thickness of the press-coating on this tablet will depend, of course, on its pharmaceutical application; the properties of the press-coating will be affected by the granulation being press-coated around the core tablet and the accuracy of the machine which performs this operation.

As many of you know, the tablet-within-a-tablet is not actually a brand new development. A patent for a pill machine which was to compress a coating upon the core tablet was granted back in 1897 to a Parker J. Noyes of Lancaster, New Hampshire. Through the years, various experiments have been made with press-coated tablets both in this country and abroad, but there was little real interest in this type of tablet until about the last year or two. This lack of interest may have been due to several factors: The crudeness of early press-coating presses, lack of information on suitable coating granulations and ways to prepare them, and perhaps even a lack of applications for these press-coated tablets.

So much for the historical background of the tablet-within-a-tablet. Some typical applications of these press-coated tablets should help to illustrate their great potential and wide range of uses:

1. Press-coating can be applied where water cannot be used in the coating pan operation; for example, with compounds containing aspirin, penicillin, and so on. This type of application explains why the nickname of "dry-coating" has been given to the press-coating process.
2. Press-coating permits the combination of two incompatible materials in a single tablet by placing one of them in the core tablet and the other in the

*Delivered before American Pharmaceutical Manufacturers' Association, December 13, 1955.

Multi-Layer Tablets*

by Theodore J. Tsevdos
MANAGER, PHARMACEUTICAL DIVISION,
F. J. STOKES MACHINE COMPANY PHILADELPHIA, PA.

press-coating.

3. Press-coating enables the manufacturer to apply a heavy time-delay or enteric coating on the core tablets, with accurate control over the thickness of this coating and the amount of dosage to be placed in it. This is especially important when a heavy coating is desired, because it requires considerable time and expense to build up a thick coat by means of a coating pan process.
4. In like manner, press-coating may also permit the making of tablets with quicker, more accurate time-disintegration properties.
5. Press-coating can make tablets with double and even triple dosages. Vitamin tablets, for example, can be press-coated with granulations containing desirable mineral combinations. Multiple dosages can be made by first press-coating core tablets with a small sub-coating and then re-running these tablets through the press to apply a second or heavier final press-coating.
6. Press-coating also permits better product identification than pan-coating because the punches of the tablet-within-a-tablet press can mark the press-coated tablets with the desired embossed, engraved or other identifying trade mark.
7. And finally, since the tablet-within-a-tablet press can produce tablets at the rate of about 500 tablets per minute and higher, press-coating becomes very attractive as a means of reducing or eliminating the time and labor cost involved in standard coating pan operations. However, the actual extent to which press-coating can reduce or eliminate pan-coating processes will depend on the pharmaceutical products and the economics of each pharmaceutical manufacturer.

There are two basic types of tablet-within-a-tablet presses. The first basic type consists of two rotary tablet presses coupled together so that the first rotary head produces the core tablet and transfers it to the second rotary head which presses the coating granulation on it. This type of tablet-within-a-tablet press is useful in making some press-coated tablets where it is desirable to produce the core tablet and then immediately press the coating granulation on it. The second basic type of tablet-within-a-tablet press consists of only one rotary press which takes previously compressed core tablets which are fed to it from an automatic hopper and presses the coating granulation on them. This second type of tablet-within-a-tablet press is usually more flexible than the first for several reasons: Core tablets can be easily made and with good speed on any standard tablet press and then

Illustration 4.
Control panel which aids in setting up, adjusting and operating the equipment.

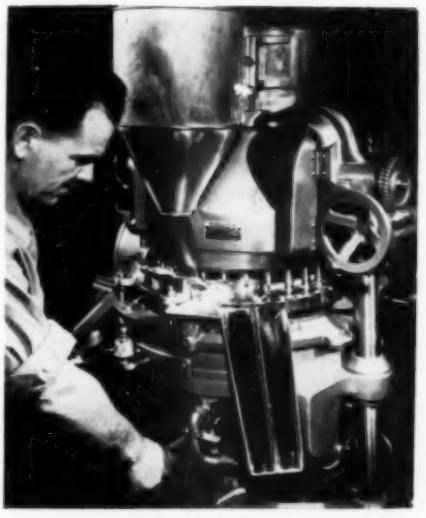


Illustration 5.
Multi-layer tablet press making accurate, two-layer tablets by individual layer-compression method.

Illustration 6.
Showing the finished two-layer tablet.

later transferred to this tablet-within-a-tablet press for the press-coating operation. This offers better flexibility in scheduling production. In addition, the necessary quality control checks can be made on the core tablets before the addition of the press-coatings.

Now let us examine a typical tablet-within-a-tablet press to see how it makes press-coated tablets and to determine its desirable features and its limitations. Illustration No. 1 shows the general arrangement of this second type of tablet-within-a-tablet press which has a single rotary head and an automatic hopper to feed the core tablets.

The core tablets are loaded into an automatic hopper which orients them and positions them into a feeder with an escapement that places each core tablet into the transfer mechanism which is located on the table of the machine. Illustration No. 2. The die is first volumetrically filled with a small amount of the coating granulation, and then the transfer mechanism takes a core tablet and inserts it and centers it in this die cavity and on top of this bottom layer of granulation. The die with the centered core tablet in it is now volumetrically filled with the remaining amount of the coating granulation, and as the die passes under the machine's pressure rolls, the punch presses the coating granulation firmly and completely around the core tablet at the proper pressure and density.

Any finished tablets that do not contain a core tablet are automatically rejected by this tablet-within-a-tablet press. The properly press-coated tablets are automatically ejected from the machine in the same way that tablets are ejected from standard tabletting presses. Illustration No. 3. This tablet-within-a-tablet press also has a convenient control panel to aid in setting up, adjusting and operating this equipment. Illustration No. 4.

Various pharmaceutical manufacturers have told us that a practical tablet-within-a-tablet press must have the following general features:

1. It must accurately center the core tablet in the finished tablet and hold variations of concentricity to within several thousandths of an inch where necessary.
2. It must be easy to set up and operate, with relatively easy changeover from one size of core tablet to another and from one type of coating granulation to another.
3. It should also be able to press-coat special shaped tablets, such as ovals, capsules, squares and so on.
4. It should be able to accurately control the thickness of the press-coating on all sides of the core tablet while pressing it to the desired pressures and densities.
5. It must be able to deliver up to 500 press-coated tablets per minute or higher, and to feed and transfer core tablets at these speeds without damaging them.
6. It must have a simple but workable inspection system that will automatically reject tablets that do not have a good core tablet in them.
7. And finally, it should be possible to operate this tablet-within-a-tablet press as a standard tablet press by simple modification when production requirements so demand.

Now, let us look at another new tabletting process with a number of useful applications, namely, the multi-layer tablet.

Multi-layer tablets are usually made with either two or three layers of material. The making of multi-layer tablets is actually a well-established industrial tabletting process. Bi-metallic contacts (which are two-layer tablets) were made by the electrical industry about 15 or 20 years ago, and three-layer pyrotechnic tablets with a red flash on top, a white illuminating charge in the center, and a green flash on the bottom were made by the Ordnance Corps over 10 years ago. But it is only recently that new developments in multi-layer tablet presses have made this process suitable for a variety of pharmaceutical applications.

As a result, pharmaceutical firms are now developing a number of new products utilizing the special capabilities of the new multi-layer tablet presses. Typical applications being considered are:

1. Multi-layer tablets are useful when two active materials must be separated by a middle layer of inert or inactive materials.
2. Multi-layer tablets may be made of two or three incompatible materials by keeping these compounds in their own individual layers in the tablet.
3. Multi-layer tablets can provide product identification by the use of different colors in the tablet layers.

Many other applications for multi-layer tablets are now being investigated by pharmaceutical manufacturers who are interested in marketing new tablet products.

Multi-layer tablets can be made by two basic methods. The older method is called the single-compression method. In this method, the die of the rotary press is filled with the different materials in successive layers, one on top of the other, and the multi-layer tablet is formed by pressing all the layers together with a single compression. With this method, the weights of each layer can be held to a variation of about two per cent or better and the separation lines between the layers sometimes tend to be a little irregular. However, this method is satisfactory for multi-layer tablet applications where very accurate weight control and clean layer-separation are not too essential.

The newer method of making multi-layer tablets is called the individual layer-compression method. In this method, each layer of material is filled and pressed separately to provide multi-layer tablets with the following advantages: First, clean straight-line separation of each layer of material; second, more accurate

(Continued on page 113)

Mode of Action of Ultra-Low Pressure Aerosols *Part one*

by Francis A. Mina, Ph.D.

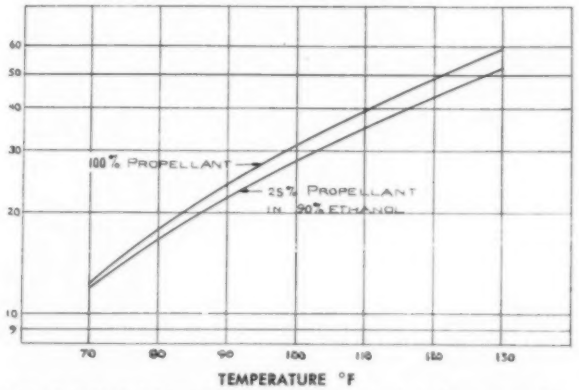
ZONITE PRODUCTS CORPORATION, NEW BRUNSWICK, NEW JERSEY.

The word "aerosol" has become less mysterious and more commonplace every day. No longer are we wont to hear pressurized products referred to as "bombs," the term generally used following commercial introduction of the first aerosols about ten years ago.

During the past decade, we have witnessed a steady progression of new aerosolized products and techniques, starting with *high pressure aerosols* in 1945, operating at pressures of approximately 70 p.s.i.g.; *low pressure aerosols* in 1947, operating at approximately 40 p.s.i.g.; *foam type aerosols* in 1950; *Three-phase System*[1] for aqueous base products in 1952, and the *Ultra-Low Pressure System*[2] for alcohol base products in 1953. The latter two developments utilize pressures as low as about 10 to 15 p.s.i.g.

But just what is an aerosol? How does it function? In other words, what makes it "tick?" It is hoped that this presentation will provide a simplified explanation of the mode of action of aerosols in general, and of the *Ultra-Low Pressure System* in particular, in the sincere belief that in understanding something about the *modi operandi*, the several aerosol principles may be utilized more widely and successfully in the drug field.

Figure 1.
PRESSURE—TEMPERATURE RELATIONSHIP
DICHLOROTETRAFLUOETHANE PROPELLANT



Note that Alcohol (as well as other solvents) tends to lower somewhat the vapor pressure of the propellant.

In this discussion, the term "aerosol" encompasses all products dispensed by means of self-contained pressure evolved from a liquefied propellent gas.

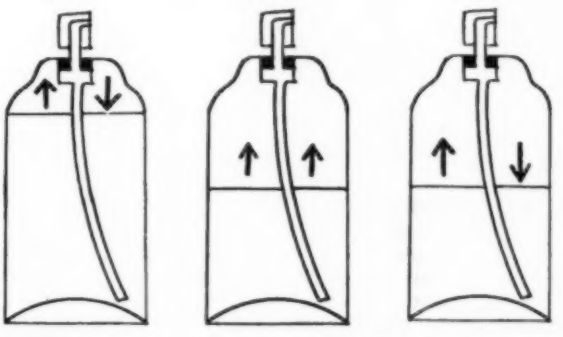
All aerosols have at least one "common denominator"—product is dispensed by means of propellent vapor acting as the driving force to expel the contents from the container.

The propellant, usually one of the low molecular weight halogenated hydrocarbons generally referred to as Freon†, or Genetron††, when enclosed in a container, maintains an uniform pressure-temperature relationship, that is to say, the vapor pressure of a given propellant remains constant at any given temperature. (Fig. 1.)

For example, an ordinary aerosol can containing, say, dichlorotetrafluoroethane (Freon 114 or Genetron 320) immersed in a constant temperature bath maintained at 70°F (21°C) will exert an internal pressure of approximately 13 p.s.i.g. As the content, i.e., propellant, is sprayed out of the can through the valve, the internal pressure will remain substantially at 13 p.s.i.g.

This is due to the fact that in an enclosed system there exists a *kinetic equilibrium* between propellent liquid and propellent vapor when the contained pressure equals the vapor pressure of the propellant at any given temperature. In other words, molecules are constantly leaving the surface of the propellent liquid in the form of vapor. The accumulated molecules of propellent vapor exert a pressure within the container and the pressure continues to build up until the contained pressure equals the vapor pressure commensurate with the pressure-temperature relationship of the particular propellant used. At that point, the number of molecules of propellant that leave the surface of the liquid fraction is equaled by the number of molecules that are returned to the liquid phase from

FIG. 2a FIG. 2b FIG. 2c



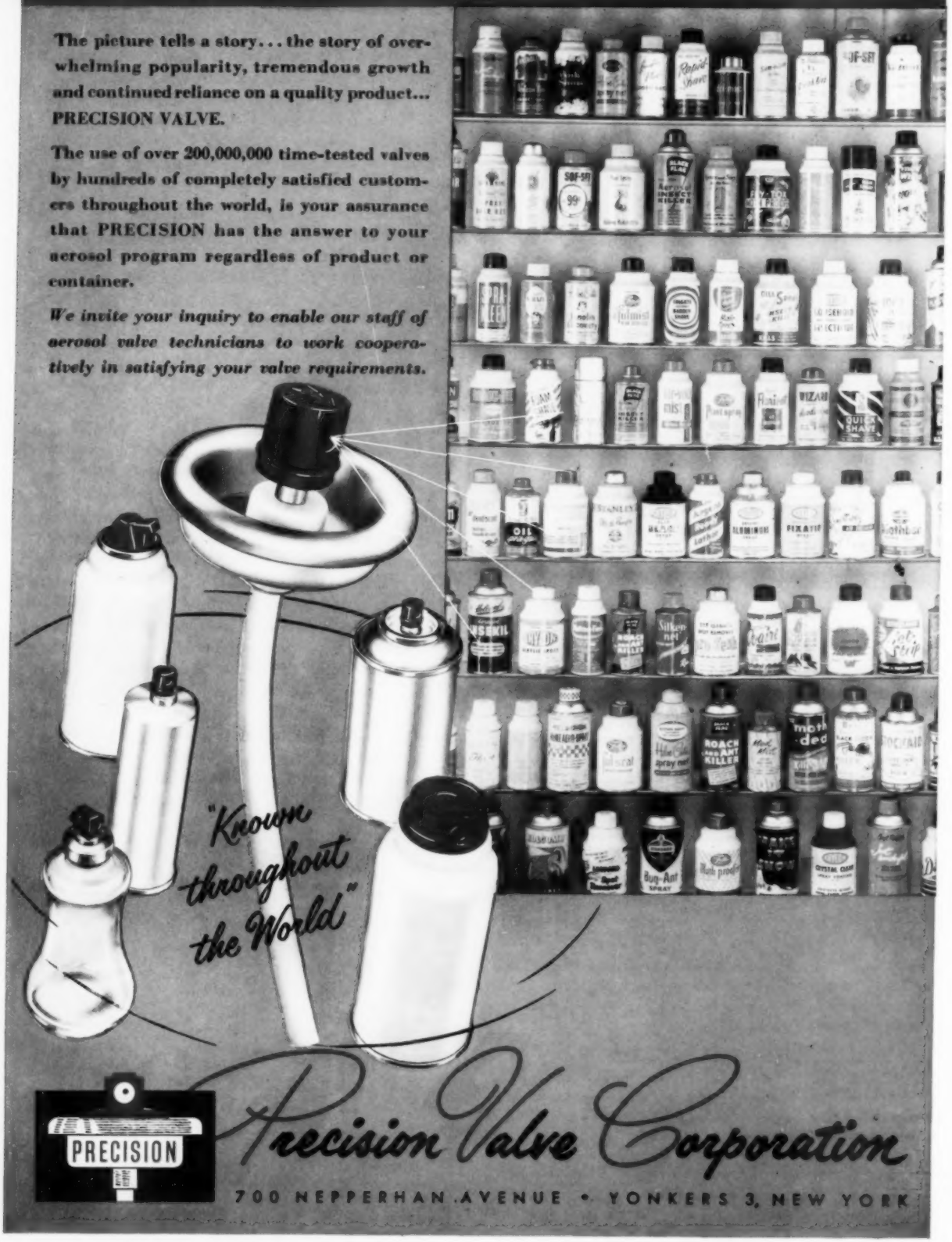
*Delivered at the American Drug Manufacturers' Association, Research and Development Section, Hot Springs, Va., Nov. 11, 1955.
†"Freon" is the registered trade-mark of E. I. duPont de Nemours & Co.
††"Genetron" is the registered trade-mark of General Chemical Co.

THE *Aerosol Valve* FOR YOUR PRODUCT *by Precision*

The picture tells a story... the story of overwhelming popularity, tremendous growth and continued reliance on a quality product... PRECISION VALVE.

The use of over 200,000,000 time-tested valves by hundreds of completely satisfied customers throughout the world, is your assurance that PRECISION has the answer to your aerosol program regardless of product or container.

We invite your inquiry to enable our staff of aerosol valve technicians to work cooperatively in satisfying your valve requirements.



Precision Valve Corporation

700 NEPPERHAN AVENUE • YONKERS 3, NEW YORK

the vapor fraction; hence, a state of equilibrium. (Fig. 2a.)

When the unit is sprayed, (Fig. 2b) the increase in head space with a resulting momentary decrease in pressure, prevents the return of the molecules of propellent vapor into the liquid phase until the contained pressure reaches the inherent vapor pressure. (Fig. 2c). The transition takes place immediately so that there is no measurable drop in pressure. This "controlled pressure," of course, increases with temperature but is constant for any given temperature.

In general, aerosols may be divided into three categories:

1) Two phase
2) Foam type
3) Three phase

Since we wish to discuss the two phase system more fully, the other two systems are described briefly at this juncture:

Foam type aerosols:

In the foam type aerosols, the propellant is emulsified in the product base so that in addition to acting as the driving force to expel the product from the container, it also whips up the product into the desired foam. This is accomplished by an internal whipping action, due to the rapid vaporization of the propellant emulsified in the dispensed product as it leaves the container and enters the relatively lower pressure of the atmosphere. This action is somewhat the reverse of beating say, egg white, where air is beaten *into* the mass. Obviously, the selection and proportion of the ingredients in the formulation impart the various desired characteristics, e.g. foam stability, lubricity, viscosity, sheen and utility.

Three phase aerosols:

The Three Phase System (Fig. 3) is designed for dispensing aqueous base products. Because of the insolubility of propellant in water, the liquefied propellant(1) remains at the bottom of the container, acting as a reservoir from which vapor forms and bubbles through the product(2) as the content of the package is sprayed.

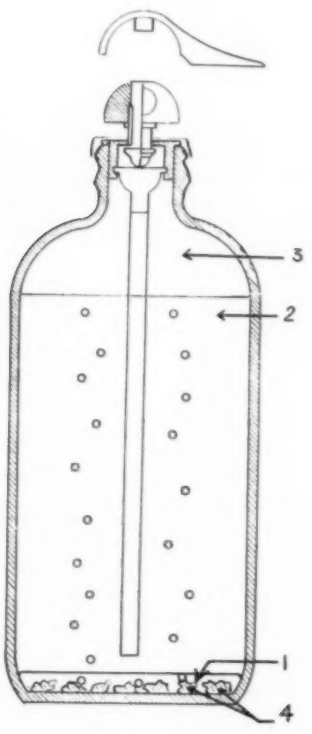
The propellent vapor in the head space(3) forces product up the dip tube and out through the valve. Note that as described earlier, the propellant vaporizes only to the extent required to achieve the normal pressure for any given temperature. However, due to the pressure-depressant action of the large volume of water base product on the propellent reservoir, there is a tendency for the internal pressure to drop considerably before additional propellant vaporizes. Under such circumstances, the vapor tends to boil violently through the product periodically, resulting in a pulsating type spray delivery. The addition of "boiling stones activator"(4) tends to minimize the lag phase of pressure build-up and allows the complete evacuation of the contents at a uniform spray rate with gradual and gentle vaporization of propellant.

Two phase aerosols:

The Two Phase System embraces those pressurized products consisting of a liquid phase composed of product base and liquefied propellant that are mutually miscible, and a supernatant phase of vaporized propellant. When the product is dispensed and the head space increases, with a resulting momentary reduction of internal pressure, propellant vaporizes out of the liquid fraction as described above (Fig. 2), to maintain an almost continuously uniform pressure.

(Continued on page 96)

FIG. 3



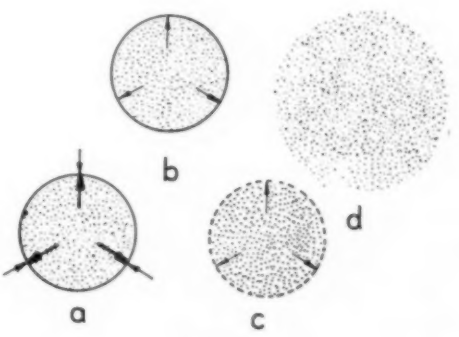


FIG. 4

Stippling represents portion of product dissolved in liquefied propellant (circular area).

a). Potential droplet of propellant-product within aerosol container prior to spraying. Arrows indicate pressure within container maintains propellant in liquid phase.

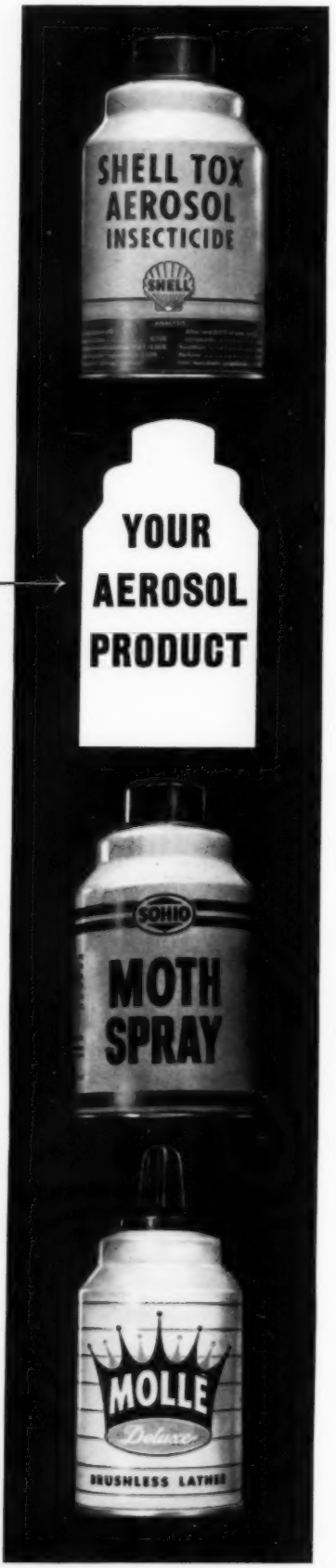
b). Droplet at time of spraying; container pressure no longer present and equilibrium disturbed.

c). Outward vaporization of propellant begins to disrupt droplet.

d). Propellant completely and rapidly vaporized, dispensing finely divided product over relatively large area.

It takes pioneering "know how"

to qualify for such
an illustrious family
and *Regal* is
ready to build it into →



No distributor should jeopardize the successful sale of his product in pressure propelled containers. And he won't if he's sure he gets *long-term* experience in this highly technical field.

Since aerosols were discovered, Regal pioneered every inch of the way. Among many firsts, Regal was the first to employ *statistical quality control*— an outstanding step in uniformity of product.

Yet Regal has never stopped pioneering. Example: the tremendous strides of "fragrances" in aerosol form are largely due to Regal research and development. Sooner or later you'll be in the aerosol field —and *now* is the time to think about it. Let Regal help you to get launched, or improve your position, right now.

We have a clear, concise story. Learn how our "know-how" can help you. Call or write

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Chemical Corporation
115 Dobbin St., Brooklyn 22, N. Y.

The Importance of Today's Package

The New York Sales Executives Club held a Packaging Clinic on December 6 at the Waldorf-Astoria Hotel, during which eight packaging experts discussed new packaging techniques. The panel answered questions on many phases of packaging during the two-hour period, ranging from the increasing importance of color and design to the necessary partnership between the carton maker and the product manufacturer.

During a luncheon prior to the clinic, O. Parker McComas, president of Philip Morris, Inc., stated that packaging is now a top management function and went on to describe his firm's recent changes in the packaging of Philip Morris and Marlboro cigarettes. George Weissman, vice-president, reported in detail on the success of the Marlboro tip-top box which was one of the most important factors in the 5,000 per cent increase in sales in less than a year.

Members of the panel were W. J. Alford, III, president of Alford Cartons; Egmont Arens and Frank Gianninoto, package designers; Albert Kner, director, design laboratory, Container Corporation of America; Louis Cheskin, director of Color Research Institute; Richard J. Walters, member of the executive committee of the U.S. Printing & Lithograph Co.; Wray Callaghan, eastern sales manager, Robert Gair Co.; and Burns W. Roper, partner, Elmo Roper & Associates.

Each member of the panel was asked a question on one facet of packaging.

***What more** can the box or carton maker do for us than we are already doing for ourselves in all the areas which affect packaging . . . design, research, line planning and so forth?*

W. J. ALFORD III, PRESIDENT OF ALFORD CARTONS

No matter how extensive your efforts and study of all areas of packaging may be, the progressive carton supplier can still help immeasurably. He can provide for you a professional objective packaging point of view which may in ways that might surprise you, save great difficulty or create potentials for you that you might otherwise have missed.

The modern role of the box, bag, or carton maker has developed over the past few years as the result of three major packaging factors:

1. As creative packaging design and construction develop, they become more complex . . . more demanding relative to the capabilities of raw materials, printing and cutting processes, finishing and sealing mechanisms and all the other hundreds of devices in fairly common packaging usage.
2. The economics of packing rest just as much on packaging line efficiency as on sales appeal. Put another way, it has become the responsibility of the prime container maker or contractor to be sure that the package runs good as well as looks good.
3. The carton maker is almost always the only member of the packaging supplier group whose success depends on rendering a continuing and comprehensive packaging service to the customer.

The machinery supplier has an essential one-time interest and the manufacturers of adhesive and other supplies are of importance but limited concern. The methods and personnel training are incidental or at least internal, but the box or carton maker—as he wants it have a really successful packaging operation—must enter into what amounts to a packaging partnership with him. He will provide staff and facilities which will render continuing service.

And so the carton maker will, if given the chance, do far more for a customer than the customer might suspect or expect.

He is best qualified to advise the customer on the suitability of a design relative to the capabilities of the machines which must produce the package. He

You CAN Add an AEROSOL Line . . . and without spending a dime for plant or equipment

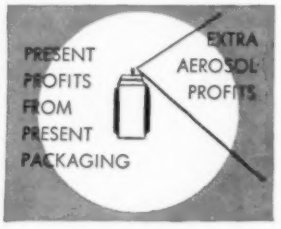
Now is the time to evaluate your product for "push-button" dispensing. Aerosols are booming. New applications for appealing, self-spraying packages are being discovered every day. If you are presently marketing your product in liquid form, the chances are you can also package it as spray or foam. Your product deserves analysis now, so we suggest you arrange with us for a free, comprehensive laboratory report. On the physical side, Continental's complete production, laboratory, and warehousing facilities eliminate any capital expenditure on your part. We do not merchandise packaged items of our own. Our sole operation is filling containers with your products . . . liquid, pressurized, or aerosol. Write today.

PRODUCTION. Continental operates 2 modern plants. Facilities will handle oil and water-base products, and refrigeration, pressure or liquid filling in any quantity. You expand sales . . . but invest nothing.

LABORATORY. Product, container, and valve research plus a tight system of quality control assure perfect product performance. We meet I. C. C. specifications and other regulations for your protection.

HERE'S HOW TO ENTER THE BOOMING *Aerosol Market* ...USING OUR INVESTMENT

WAREHOUSING. Ample bulk storage space enables us to keep a good supply of your ingredients available at all times. Drop shipping in bulk lots. Use our Midwest plants as central distributing points.



Aerosol packaging may mean a bigger market for you. Aerosols adapt to perfumes, deodorants, medicines, insecticides, household chemical specialties, etc. Get our report now!

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CONTINENTAL FILLING CORPORATION

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is best qualified to work with the customer's production people, on a day to day partnership basis, on the packaging line; adjusting machines, glues and methods to run packages best, or adjusting package specifications to match machines.

Many customers know only too well the value of such a packaging partnership as measured in low down time, fast service, and real know-how to add to the abilities of his own production people.

How does the Art Director's work tie in with Marketing Research?

ALBERT KNER, DIRECTOR, DESIGN LABORATORY, CONTAINER CORPORATION OF AMERICA

Since a package design is a solution to a merchandising problem, it is imperative to provide the Art Director with all significant data bearing on marketing: **1.** physical characteristics of the packaged product; **2.** distribution methods; **3.** price structure; **4.** competitive products.

The design itself must be a composite of many elements with varying functions. A surprisingly large number of design elements are measurable quantities and can be scientifically evaluated. These include legibility, color recognition, identification of design form, impact appeal, and eye attraction.

To create an effective design, a Design Department must dwell on two phases of research: **1.** the marketing structure of the product; **2.** the principles of commercial design. But remember that while effective design is based on research, no scientific studies can replace the creativity of the commercial artist.

How do you evaluate color and solve color problems in designing and redesigning a package?

LOUIS CHESKIN, DIRECTOR, COLOR RESEARCH INSTITUTE

We evaluate colors as such by making use of accumulated data obtained from tests with thousands of consumers conducted on an unconscious level.

We solve specific color problems by using procedures and techniques that are designed to reach the unconscious or subconscious mind, because rarely are the consumers aware that they are influenced by the color or design of a package. In fact, if people are asked direct questions concerning the color or design of a package, the answers are biased by the desire to give the impression of having a logical or practical mind and good taste.

Actually, consumers generally react emotionally to the color, imagery and design, which in the subconscious they associate with the product or brand.

Because consumers transfer the sensation from the package to the product or brand without being aware of it, they cannot tell us anything about the relationship between the color or design on the package and the product itself, and we must, therefore, conduct the tests so that we can obtain spontaneous and natural responses that reveal true attitudes, favorable and unfavorable.

Unconscious level testing techniques enable us to get consumers' natural reactions. They make possible for us to have testing conditions similar to a shopping situation, in which the consumer is not conscious that she is influenced by the package.

Are there any new printing techniques that help in package design?

RICHARD J. WALTERS, MEMBER OF EXECUTIVE COMMITTEE, U. S. PRINTING & LITHOGRAPH CO.

Yes, there are many new printing techniques which have contributed to improved package design in recent years. In this connection, it is well to keep in mind this basic fact—that no design, no matter how elaborate or how well conceived is of any value unless it can be reproduced millions of times on a practical and economical basis that will meet the standards of our system of mass production and distribution as we know it today.

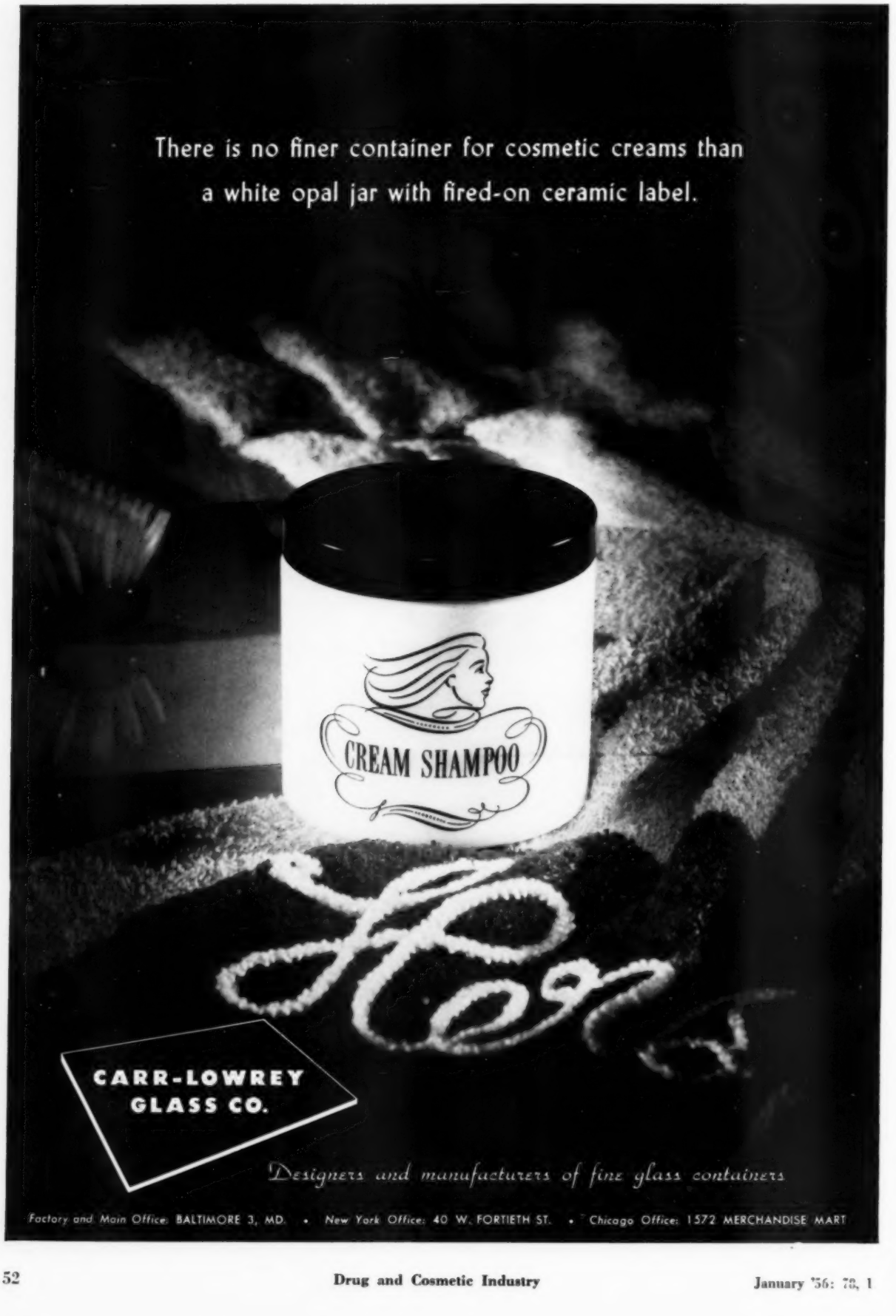
Now the graphic arts industry has done many things to make this possible. Obviously it would be impossible to even begin to tell you about them in the limited time available here. The best I can do is mention a few.

Perhaps two basic improvements stand out above all others. One is the improvement of printing surfaces of folding boxboard and paper used in packaging. The other is the improved plate making techniques which make it possible to secure realistic full color effects in the reproduction of halftone pictorials with four basic process colors. Today, the quality of this reproduction on packaging materials is as fine as any color printing being done in any other media—and it is done at high speed and at economical cost.

A fine example of what these improvements have meant to packaging can be gained from the food industry. A visit to any modern supermarket will demonstrate what I am talking about. What the graphic arts has done to help improve packaging design is certainly apparent from the many examples of fine color reproduction on supermarket shelves today.

By way of illustrating the results that can be obtained from packaging design improvement, I would like to cite an example in the food industry. Not too long ago General Foods decided to improve the package designs for Minute Rice and Minute Tapioca. For years these products had been merchandised in simple two color cartons. The new designs went from two colors to four colors and utilized full color reproductions of a series of food pictorials illustrating novel servings of the product. The new designs were prepared and tested and the results were amazingly successful. Sales increased sharply. Impulse buying of the products was spurred through greater product recognition and the sales appeal of appetizing full color food servings and accompanying recipes. This example is typical of many in the food industry which,

(Continued on page 96)


There is no finer container for cosmetic creams than
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Packaging and Selling

Self-Competition

Among the many new ways of life that are the order of the day in this new and wonderful world of ours are some drastic changes that are taking place in marketing.

Undoubtedly, the basic reason that these changes are taking place is that America has developed into a mass-class market. Either from the viewpoint of income or spending power, the vast majority of our consumers are in the middle income range. A second social factor of this era is the eager willingness of the customer to experiment and try something new, rather than to build any of the traditional sales resistance against a new idea. This has brought about a customer fickleness and a lack of loyalty toward the established brand that is very distressing to many merchandisers.

One of the real decisive marketing developments of this new era is the tendency of big business to more and more establish fields of intense competition within its own company, its own ownership and its own control. Self-competition is probably just the opposite of diversification. These two opposite roads to bigger and bigger bigness are the primary paths used by business for greater growth.

The outstanding example of self-competition and where it shows up in its most obvious way and in all the aspects of self-competition is in the automobile business. Today almost every car looks like a Cadillac, each one is striving to emulate the Cadillac in horsepower, looks and gimmicks. But within the family name of any one single car is a range of models covering every possible consumer taste and market. Thus, in any single consumer market for a type of automobile, General Motors, Ford and Chrysler are in self-competition with several parallel brands.

In this our own trade self-competition is becoming more and more a favored way to expand, whenever the market is big enough to justify competing brands under one ownership and whenever research or advertising gimmicks or any other product differentiation opens up the opportunity.

The tooth paste field is probably the most clearly perceived product field in our industry where self-competition is working vigorously. The reason for this self-competition in the tooth paste field is of course self-protection in preserving one market, while still maintaining the flexibility to enter a new, encouraging market.

If the tooth paste people keep up their record of about one scientific miracle every two years, most of the leading companies will have an interesting collection of self-competing brands.

Procter & Gamble is probably the best example of a deliberately calculated policy of self-competition. Procter & Gamble's entry into any market is based upon exhaustive pre-testing of package, product, advertising and marketing policy. It then sweeps from city to city with the preponderant force and skill with which Caesar swept through Gaul.

Procter & Gamble have apparently developed a keen, perceptive understanding of market saturation. That is the degree of sale which any product with any specific appeal, or differentiation, reaches at some time in its marketing development. Beyond that point the advertising dollars and the sales effort become less productive and reach a point where they are not effectively earning their way. That is the viewpoint where Procter & Gamble has been wont to introduce another product, of different character and appeal, providing the market has been big enough to sustain additional effort for worthwhile rewards. Probably the best example of Procter & Gamble's self-competition is the big family of well to do and poor relations gathering around Crisco.

Self-competition is of course competition in the best sense of our free enterprise society. Nevertheless, now that the Federal Trade Commission is looking at monopoly from the viewpoint of a product as well as a group of products and also as well as industry-wide, as shown in a recent situation following a merger in the pharmaceutical industry, we wonder whether the self-competition of some of our companies in certain products fields is not also approaching the legal saturation point.

Gimmicks

Here's what the executive of a leading super-market said recently to some food manufacturers. These thoughts could with equal reason be presented to many manufacturers in this trade.

"Continued use of gimmicks as promotional devices by national manufacturers contributes little or nothing to the building of brand loyalty. They do not seek to convince the consumer of the merits of a product or to establish convictions that are a fundamental essential to brand loyalty."

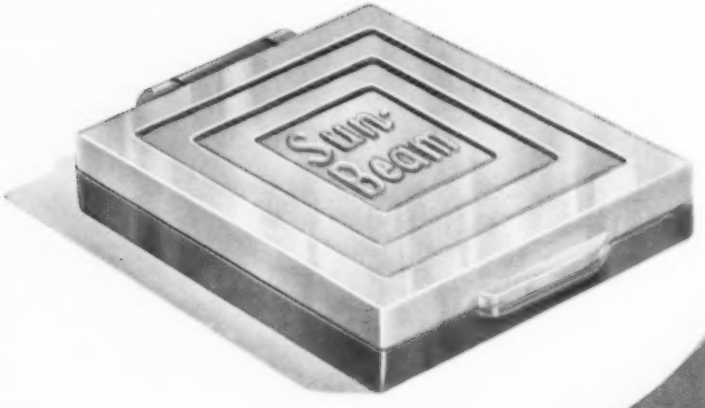
The Rectal Route

Anyone who believes there are no horizons in sight for the pharmaceutical industry, or to put it another way, that there are any market limitations or barriers, should study the announcement of one of our newest pharmaceutical companies, that is the Miller Laboratories, Inc. Samuel Miller, the President, who was recently Executive Vice President of Schenley Laboratories, Inc., and a former director of Marketing with the advertising agency Lord & Thomas, provides a living example of the drug industry's ability to pioneer new avenues for market exploration.

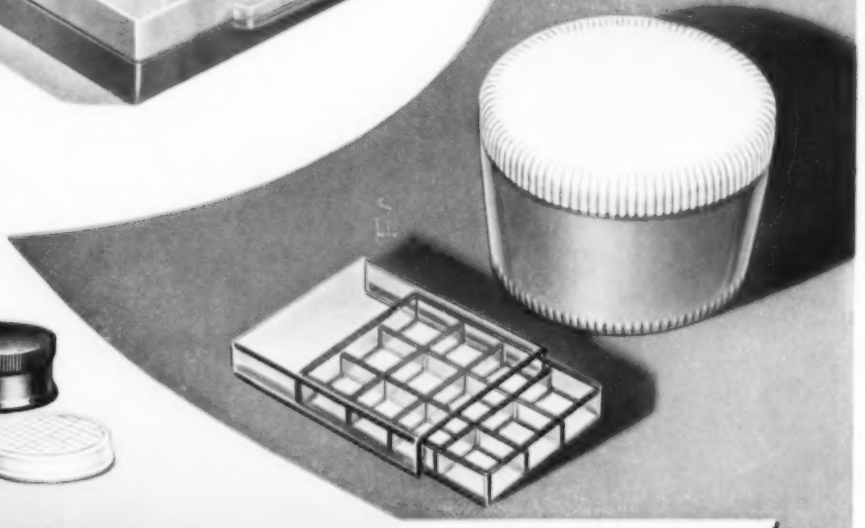
Said Mr. Miller: "Our techniques of developing the rectal route to therapy gives promise that many new

For precision and versatility—choose
OWENS-ILLINOIS for PLASTICS

For example—
A lady's compact



For example—
Cosmetic jar and tablet container.



For example—
Fitments for glass, plastic, metal and paper containers (slip caps).

Owens-Illinois packaging know-how and high-quality standards offer you the *finest* in molding plastic facilities . . . Injection molding . . . Compression molding . . . A complete range in plastics for packaging, for specialties.

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Birmingham . . . Alabama	Detroit . . . Michigan	New Orleans . . . Louisiana	St. Louis . . . Missouri
Boston . . . Massachusetts	Fresno . . . California	New York . . . New York	St. Paul . . . Minnesota
Buffalo . . . New York	Houston . . . Texas	Oakland . . . California	Salt Lake City . . . Utah
Charleston . . . West Virginia	Indianapolis . . . Indiana	Oklahoma City . . . Oklahoma	San Francisco . . . California
Charlotte . . . North Carolina	Jacksonville . . . Florida	Omaha . . . Nebraska	Seattle . . . Washington
Chicago . . . Illinois	Kansas City . . . Missouri	Peoria . . . Illinois	Toledo . . . Ohio
Cincinnati . . . Ohio	Los Angeles . . . California	Philadelphia . . . Pennsylvania	Yakima . . . Washington
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drugs producing undesirable side effects when given orally or by injection can now be used with safety, convenience and comfort for the patient."

Of course, it is too early to guess how dense traffic will be on the "rectal route" but we have no doubt that it if this proves to be a roadway to the promised land of more profits, that several other pharmaceutical companies will be impatiently jostling each other on this busy roadway."

Something New

We note with interest that Pabst is bringing out a new quart size container with a great hurrah and hurray. In this industry, which has been long used to the jumbo size, the economy size or even to the thousand dollar quart bottle perfume, this promotion creates no excitement. It just seems to point out to the general idea that today you must always do something new. It does not seem to make very much difference what you do that is new so long as it is different.

Declining Drug Store Sales

In a recent speech, at a drug convention, a leading executive of Colgate-Palmolive Company gave a grim review of the toilet goods sales gains in grocery stores and then offered his solution to the retail druggist.

According to this executive, the $4,900,000,000 sales of drug stores for 1954 represents an all-time sales peak. These growing sales of the drug store have served to conceal and minimize the fact that the chain super-market and the independent food stores are now selling many toiletries such as tooth paste, shampoo and other items that were formerly only available in the retail drug store.

During 1954, the food stores in this country retailed $700,000,000 in toiletries and packaged proprietaries, a figure that has actually doubled the volume done only two years before, that is during 1952. Also in 1954, the health and beauty aid business through grocery outlets was approximately 15 per cent of that done by drug stores in all commodities. Actually, those goods that go to make up the health and beauty aid department of the retail grocery store today are actually the items and lines that at one time accounted for as high as 31 per cent of the total drug store business.

Examining the sales trends of 25 volume toiletries and proprietary commodities, we find that during the last three years, the sales of these top volume brands being made through retail food stores has increased 62 per cent whereas through drug stores the increase was three per cent.

Another and more disturbing picture is that of consumer buying habits. Using tooth paste as an example, we see that in 1945, just ten years ago, out of each hundred people buying tooth paste 73 bought their tooth paste in the drugstore with only eight buying through the food outlet. Today, in 1955, ten years later, we see only 34 out of each hundred buying their tooth paste in the drugstore and 60 out of each hundred are buying their tooth paste from the food retailer. These leading toiletry items should properly be classified as impulse items, probably more correctly as high velocity merchandise in which purchasing is influenced by the subconscious mind, with 71 per cent of the total sales volume of such goods being classified as impulse sales. It is a fact that during 1955, 75 per cent of the total retail sales of all tooth pastes, shampoos, home wave kits or oral antiseptics, plus other top volume toiletries and a high percentage of the packaged proprietaries will be sold from open display shelf and selected display.

This is in fact a grim picture for a historical group of products that for many years have traditionally belonged in the drugstore. That the trend away from the drugstore into the super-market has been a swiftly mounting one, we do not need this toiletries executive to tell us. As products of this industry become more and more low priced, functional necessities and therefore almost entirely impulse pickup items, it would seem that this trend toward greater super-market sales will continue.

Another factor which favors the super-market and which we do not see discussed anywhere, is that in an increasing number of smaller cities, towns and villages, there are now several modern efficient super-markets and one or two or three as the case may be, drug stores, which have shown little change or improvement in the last ten or twenty years. In other words, the modern super-market is a highly efficient glamourous streamlined distribution operation. It is generally everywhere invading the smaller towns and it is generally meeting old-fashioned retail drug setups. We do not particularly like the prescription of this executive to help the druggist meet this competition. This prescription is to select only the top volume brands in each classification for exposure to the public. This executive believes that the display space for a group of products such as tooth paste, for instance, should be based upon their turnover in relation to other products such as shampoo and that within this classification only the top four brands should be given display. According to this executive, in any branch of this part of the toilet article or proprietary field there are four brands that will make up about 85 per cent of the total dollar sale. For instance, if tooth paste sales are taken at 100, then shampoos, the second largest group enjoy 75 per cent of the tooth paste volume, the home wave kits and refills run at 53 per cent, hair tonic, 35 per cent; tooth brushes, 34; dedorants, 37; hand lotions, 28; shaving cream, 32; oral antiseptics, 32, etc.

This group display, with the limitation of brands to the top leaders, makes a very neat arrangement and is the exact formula used by the rack jobber for the products of this industry which he sets up in grocery stores.

To say that this is the solution for a drug store to save this part of the business is, we think, open to strenuous debate. We do not think that the druggist has the kind of a store, the community reputation or any other factor which would turn him into rack merchandiser of toilet articles. In fact, we suspect, and we have long stated on other occasions, that there are so many fields of profitable business development

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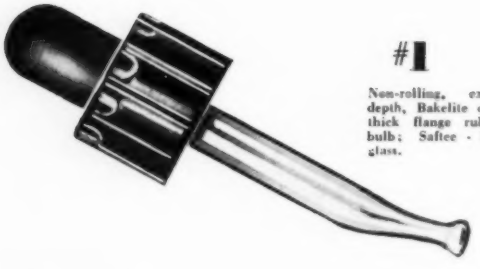
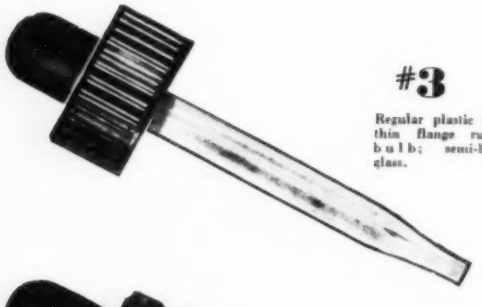


#1

Non-rolling, extra-depth, Bakelite cap; thick flange rubber bulb; Saftee - ball glass.



#3

Regular plastic cap; thin flange rubber bulb; semi-blunt glass.

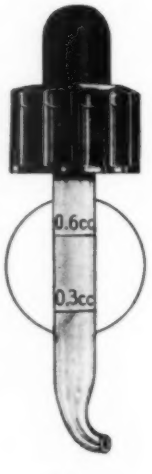
#4

Metal cap; oil-resisting Amekine synthetic rubber bulb; blunt glass.

By the Originators and World's Largest Manufacturers of Screw-Cap Dropping Parts

Since 1931, when the screw-cap dropping part was originated by Pennsylvania Glass Products, the world-wide acceptance of New Perfection has been increasing. The fact that the New Perfection Dropping Part is the most practical and sanitary dispensing unit for liquid preparations accounts for its popularity and the steady growth of our operations is due to the efficiency with which our products are manufactured and distributed.

Our exacting standards for quality, uniformity and cleanliness guarantee that each shipment will meet your most rigid specifications. Our policy is to produce and sell the best in dropping parts—and thus merit your continued patronage in the future as we have in the past.



#2

Non-rolling, extra-depth, Bakelite cap; thick flange rubber bulb; special bent glass (CALIBRATED in color)

New Modernistic bottle. Designed to lie flat for convenient labeling. Oval front provides ample label space.

New Perfection Dropping Parts, either plain or CALIBRATED IN COLOR, can be supplied to fit your bottle or with our new Modernistic style bottles. Our bottles are available in Amber, Blue, Green or Clear glass in ⅛, ¼, ½, 1 and 2 oz. capacities. Special oil-resisting AMEKINE synthetic rubber bulbs can be supplied for use with oil products, or natural rubber bulbs for general usage.

Write for Samples and Quotations

PENNSYLVANIA GLASS PRODUCTS CO. INC.

"Glass Goods of the Better Kind"

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opening up to the drugstore, that is fields which do not in any way parallel anything the grocery stores can do, that the intelligent druggist who has any instinct for merchandising can well afford to let such things as tooth paste slip to a minimum and unimportant part of his sales.

So long as the druggist has such unexplored divisions such as animal health, plant health, nutrition and others to experiment with, he should not worry too seriously about these mass-distributed, impulse, low-priced, pickup products.

How to Tell a Good Trademark

No one in this industry needs to be told that a trademark is a vital part of their business. They also do not need to be told that there are good trademarks and poor trademarks as well as efficient trademarks and inefficient trademarks.

In spite of the fact that we are so overwhelmingly trademark conscious, it seems to us that it would do no harm at all to repeat here the elements of a good trademark as laid down by Jim Nash of Jim Nash Industrial Designers, New York at a recent meeting of the Society of Industrial Packaging and Materials Handling Engineers.

Here are the five jobs that a trademark should do for its product:

They must:

1. Assist in catching consumer attention.
2. Furnish strong brand identification among many packages.
3. Instill confidence in products because salesmen are no longer closely associated with them.
4. Give complex product lines a family resemblance.
5. Tie all the advertising together at the point of purchase.

Mr. Nash then went on to suggest several rules for judging the value of a trademark. Among them were:

1. Don't use overworked geometric shapes as the major design.
2. Don't rely on color for legal protection.
3. Make the mark interesting, individual and pictorial.
4. Use strong design rather than color for memory value.
5. Try to have a mark that can be thought of and described in a few words.
6. Design the mark so that it can be printed easily in b&w and various color combinations and on various surfaces.

Which?

Splurge or consistency? That's the question *Printers Ink* Sales Executives Clinic members were asked in regard to company advertising, and ads that primarily support salesmen (trade magazines). Answers: Consistent 70 per cent, splurge two per cent, both 19 per cent, depends nine per cent.

In other words, the splurge (peak advertising, multiple inserts or pages, etc.) is good, but only if it is first supported by consistent month in and month out advertising.

Headline

Our favorite headline for this Xmas: "Promise Her Anything, But Give Her Arpegè."

This Wonderful Country

Ponderous problems propagate in the food industry. Just now the "Birds Eyes" boys are palpitating with the problem "Are We Handling the Big Pot Pie Potential Right?" Keep at it fellas, you gotta be right.

Potent Influence

According to a recent study, word-of-mouth is the most under-rated force in influencing people. Results of a detailed study of four groups of decisions by 800 women showed that personal influence is considerably more potent—both as to "exposure" and effect—than mass media.

Selling Women

Here are some figures from the Metropolitan Life Insurance Co. There are 40 million married women, of whom 16 million are under 35 and another 10 million in the 35 to 44 age group. About 10,700,000 of them work outside the home.

Super-Facts

What makes a super-market give shelf room to a non-food product. In a recent article in the *Wall Street Journal*, some of the big super operators are quoted on this subject.

"We have a rather simple Yardstick" says Lansing P. Shield, president of Grand Union Co., an Eastern grocery chain. "If we can give the customer a real supermarket value on the item, if it is used up in a reasonable length of time in the home or by the family, and if the style element is not important then we are likely to stock it."

L. P. Shinn of J. Weingarten, Inc., Houston, says "non-food offerings must be staple, repeat items that can be easily packaged, and they must be in great demand so they won't get stuck on the shelves."

Louis Stein, president of Food Fair Stores, Inc. says that "non-food items the chain is interested in carrying must have a turn-over as rapid as its food products; its food inventories turn over about 20 times a year."

"According to William Golub, president of Central Markets, Inc., Schenectady, N. Y. Slow movers among the groceries must be stocked because the housewife expects you to have a complete line, but in non-foods there is no room for shelf warmers."

"Customer traffic in supermarkets is different from other type stores," says another supermarket operator. "The basic difference which determines the non-food items a grocery can merchandise, is the pattern of new versus repeat customers."

"Almost all supermarkets' customers come in at least once during a six-week period, while a department store gets new customers all year."

(Continued on page 60)

We Proudly Present

CALUMET'S NEW KING SIZE

Swivelpak®

THE ORIGINAL AIR-TIGHT, PROPEL, REPEL CONTAINERS, NOW IN 3 SIZES!

Here's the Big Boy — the 1½ ounce Super King Size of the famous Calumet Line of Air-Tight, Propel-Repel Plastic Containers.

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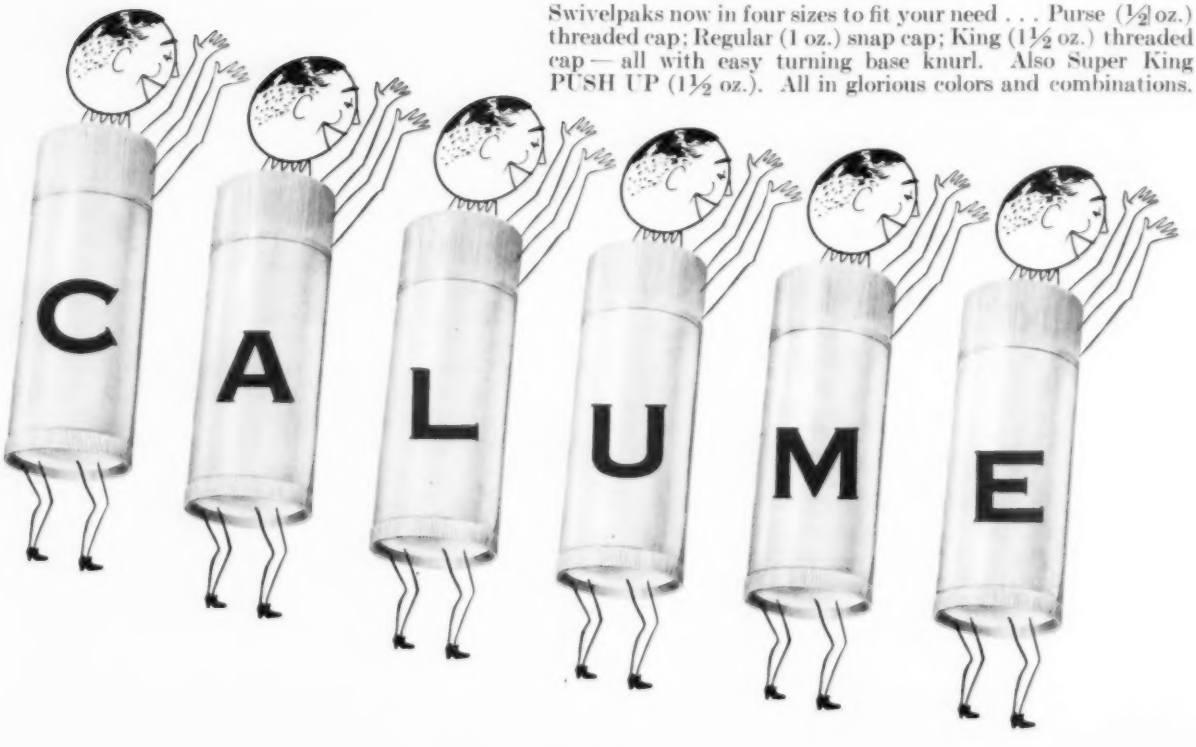
Swivelpaks now in four sizes to fit your need . . . Purse (½ oz.) threaded cap; Regular (1 oz.) snap cap; King (1½ oz.) threaded cap — all with easy turning base knurl. Also Super King PUSH UP (1½ oz.). All in glorious colors and combinations.



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565 Fifth Ave., New York 17, N. Y., MU 8-4270.

In Canada, Calumet Division of Eric H. Hardman Ltd.,
137 Wellington St., West, Toronto, Canada.

(*Continued from page 57*)

"This means that unless you have something that is consumed or used up, your item goes dead in a supermarket after a six-week period."

"We don't want anything that can be pilfered easily or that slips through the basket of the wire buggies, and we try to avoid any item that retails above a dollar," said another operator.

Still another operator: "We don't stock any items that have an element of risk in them, such as a fashion aspect or are good for only a short selling season."

"We rotate our items in order to get the maximum sales out of the rack space available. In any one store during a year's time we offer about 3,000 items, but no more than 150 at any one time. When sales of an item start to fall off, we quickly move it out and replace it with one that will sell."

These comments seem to us to be a good summary of the facts of life in super-market selling—some facts that a good many ambitious members of our industry may well ponder over.

Point of Sale Aid

According to the manager of the Sales Promotion Group of the National Retail Dry Goods Association, retailers are using only a small proportion of the sales aids furnished by manufacturers.

Here is a 10-point check list to assist manufacturers in obtaining better retail cooperation furnished by this executive.

1. Use the retail slant in store aids.
2. Make retail aids flexible.
3. Give store facts about merchandise.
4. Provide stores with sales training material.
5. Furnish stores with good art work or photographs.
6. Design retail advertising to look like store advertising.
7. Produce mailing pieces with a retail angle.
8. Create display material and ideas which are practical for the store to use.
9. Time promotional material properly.
10. Route the material to right person in the store.

According to this man, manufacturers should be careful to distinguish between large stores and other stores. Large stores, he says, want photos and art work, other stores want mats. Big stores want ideas, smaller stores want a complete promotion kit.

Point of Purchase

Here is how an expert on point-of-purchase sales aids lists the relative importance of the major factors which must enter into this sales material:

(A) Must attract attention by color, copy, lighting and placement. Most buying is done by sight. This makes the color and readability of primary importance.

(B) Should show product in use. Visual presentation of merchandise and its benefits gets people to look. When features are dramatized and emphasized prospect learns something about the product. When they act on what they learn the sale is made.

(C) Must be planned for specific purpose and location.

(D) Must add to prestige of product and of retailer.

(E) Arouse desire and stimulate impulse to buy.

(F) Be easy to use.

(G) Should stimulate related sales (tooth paste vs. tooth brushes, shirts vs. ties, pipes vs. tobacco, pillow cases vs. sheets).

To meet these requirements (point-of-purchase material) should:

(1) Have human interest.

(2) Have unusual shape or material.

(3) Attract traffic to product.

(4) Use skyscraper space instead of width or depth.

(5) Make store more interesting.

(6) Show trademark and price.

Vanity or Health

The President of one of the largest food companies believes that the answer to the further booming sales of dietetic food products is to emphasize vanity rather than to put all the emphasis on health, such as has been true in the past.

Said this food leader: "There seems to be every reason to believe that the increased demand is coming not only from those who are worried about overweight from the standpoint of health, but also from those whose vanity demands a slim, youthful figure . . . men as well as women.

This seems to us a very intelligent market analysis which can well expand the consumption of dietetic foods. It is of course completely true that dietetic foods, in addition to their place as part of the treatment for numerous illnesses, are also serving vanity in improving personal appearance.

We think it very likely that some analytical thinking in the pharmaceutical industry could just as well add the potent human buying motivation of vanity to their expanding sales, as well as that of health.

Short Time Popularity

In its past history, the perfume and cosmetic industry has had some unpleasant experiences in tying in its product, either by the name of the company or the product brand name, with some famous current notable. We don't have to go back very many years to recall the products or the companies whose names were associated with famous Hollywood stars, famous actresses or other famous personages. In every case, so far as we can recall now, this association with the name of a living prominent personality gave only a brief life to the associated commercial product.

To give a vivid example of the danger of association with any name that reaches a quick and sudden peak of popularity in this responsive and ever changing American market, we offer you the experience of Davy Crockett.

A leading research organization has just completed a survey among 3615 kids, from four to 14 years of age regarding the popularity of Davey Crockett. They state that only 15 per cent of the kids failed to give Davey the horse radish. For this reason, this research organization is advising a toy client that the Crockett popularity will fall through the floor before the Christmas market starts.

NEWS IN PACKAGING...

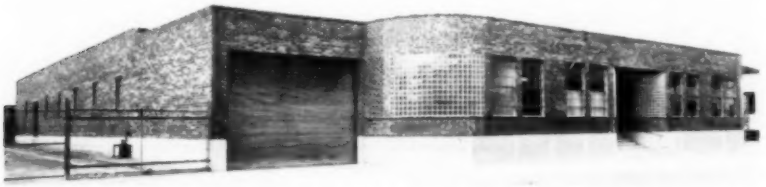
Barr Opens West Coast Plant

Operations have begun in the new Los Angeles installation of G. Barr & Co.'s plant. This is the firm's third plant, according to George Barr, president.

The West Coast plant, like those of Chicago and New York, includes equipment for both refrigerated and pressure filling. It also has its own quality control laboratory.

Nosco Promotions

Charles Kufner has been promoted from superintendent of plant and production to general superintendent of Nosco Plastics, Inc., according to Harry Kugel, president. William Hayes, process engineer, has become superintendent of molding; Robert Mangold, foreman of folding, has become process engineer; and George Jowels has been named foreman.



New plant of G. Barr & Co., Los Angeles, which is now in production. As in Chicago and New York plants, the West Coast addition includes equipment for both refrigerated and pressure filling as well as its own quality control laboratory.

Testing Corrugated Boxes

Hinde & Dauch has issued a new edition of its Little Packaging Library booklet, "How to Test Corrugated Boxes," which is designed to acquaint producers with the importance and the techniques of package testing. The booklet offers a comprehensive checklist to help the packager judge qualities of specific corrugated boxes. New material has been added in order to bring it up to date on modern testing procedures.

Copies may be obtained by writing to Hinde & Dauch, Sandusky, Ohio.

Amer. Viscose Appointments

Howard P. Heilman has joined the film division of American Viscose Corp. as a salesman in the Chicago office, according to J. W. Little, sales manager. He will handle the sale of Avisco sheet and roll cellophane on the southern side of Chicago and in Gary and Hammond, Ind.

Thomas W. Trainer and Richard E. Glenn have been transferred in the film division, with Mr. Trainer moving from the technical service department in Fredericksburg, Va., to the company's new warehouse in Los Angeles. Mr. Glenn, formerly a salesman in Chicago, has been transferred to Western and Northern Michigan.

Michael Lemmermeyer, left, president of Aromatic Products, Inc., standing before an exhibition of his paintings displayed at Chemical Specialties Manufacturers Association Convention last month in New York. With him are H. W. Hamilton, C.S.M.A. secretary, and Dr. E. G. Klarmann, right, Association president.

Barnett with Wilson Glass

Raymond Barnett, formerly vice-president of Old Empire Inc., has been appointed general sales manager of J. W. Wilson Glass Co., Inc., according to Griffin Crafts, president. He will also manage and coordinate sales of Wilson Plastic Container Corp. and Baltimore Metal Products, Inc.

Daniels Promoted by Gair

John W. Daniels has been promoted to superintendent of the Connecticut corrugated box division at Portland, Conn., of Robert Gair Co., according to William T. May, Jr., vice-president in charge of container operations. He succeeds Joseph M. Murphy who recently became special production representative of Gair's container division.

Ham Named by Std. Packaging

Harold A. Ham has been appointed to the newly created position of general manager in charge of manufacturing at the Flex-Vac division of Standard Packaging Corp. He had formerly been associated with Hoffmann-La Roche as director of pharmaceutical production, and prior to that, with Lehn & Fink, as general factories manager.

He will assume the former duties of H. T. Holbrook as general manager.

Mr. Holbrook has been appointed to a new position as vice-president in charge of the company's expansion and growth in packaging and related fields.

Folding Carton Contest

The Folding Paper Box Association of America will hold the 11th annual folding carton competition in San Francisco from March 10 to 12 in connection with the Association's 1956 convention. According to John C. Newell, Jr., director of public relations, the 100 best folding cartons will be chosen on the basis of four points: technical superiority of printing, superiority of construction, potential new volume use, and general superiority according to end use.

All entries will be exhibited in Chicago and New York City as well as being displayed at the convention. The prize-winners will be shown at major cities throughout the country.

The competition runs from November 1 to December 31, 1955, and is open only to members of the Folding Paper Box Association of America.

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Patent THOUGHTS AND TRENDS

by Thomas Cifelli, Jr.
PATENT ATTORNEY

SERIOUS PATENT PROBLEM IN THE DRUG INDUSTRY

The drug industry now has a rather serious patent problem, one which may spread to other chemical fields. For this reason the entire article this month is concerned with just this one matter.

In brief, the drug industry has run into a serious snag in its attempt to protect new intermediates made during the course of synthesizing therapeutic materials.

The problem generally develops in some such manner as the following:

In starting out a synthesis, simple materials are normally employed and as the various steps are performed the resulting materials become more and more complex. The entire synthesis may involve several steps. As each hurdle, i. e. intermediate, is prepared there is a natural pressure applied for the inventors to publish. This is good as it enriches the common pool of knowledge. Normally, patent applications are filed on the intermediates as they are developed, usually shortly prior to publication.

Until about 10 years or so ago it was customary to ascribe a general use to the intermediates in order to satisfy patent requirements. Thus patents often contain the expression that a material is suitable for use in organic synthesis. Such broad statements of utility were accepted by the U. S. Patent Office as meeting the legal requirements.

However, this situation eventually became complicated by the fact that the Patent Office adopted the position that such statements were inadequate, on the ground that any chemical could be used in organic synthesis of some kind. To every action there is an equal and opposite reaction, and consequently the patent attorneys met this position of the Patent Office by using statements to bring out the special utility of the intermediates for the synthesis of the final desired product, such as for example, vitamin A and cortisone.

For a time this solution appeared to work out satisfactorily as it was accepted by the Patent Office and did not impose any undue burdens on the patent applicants. One of the objections to such statements was that it showed the "hand" of the applicant prematurely. This followed from the fact that it would be possible that the patent on the intermediate would issue long before it was known that the applicant was working on a particular synthesis. However, it does not appear unreasonable to say that the competitors in the drug field are sufficiently bright as to jump to the correct conclusion even in the absence of statements such as the one in question; and hence the objection was not seriously advanced.

Since the reference compound would not be suitable for the purpose needed because its chemical structure made it non-usable, for example, either because its substituents were in the "wrong" p'aces or the double bonds were unconjugated when conjugated ones were necessary, or for some other reason, it was not difficult to find an argument to support patentability.

However, this pleasant situation did not last long. The Patent Office then adopted the position that such arguments were not arguments dealing with the patentability of the intermediate per se. The Patent Office made the requirement that it was necessary to show some unobvious superior property which was possessed by the novel intermediate as compared with the reference homolog, isomer or other closely-related compounds, structurally speaking

Such a requirement meant that it was necessary to attempt to divine" what possible properties, such as anti-oxidant activity, plasticizing effect, emulsifying characteristics, etc. would show up better in the novel intermediate than in the reference compound.

Let us for a moment consider the practical effect of such rulings.

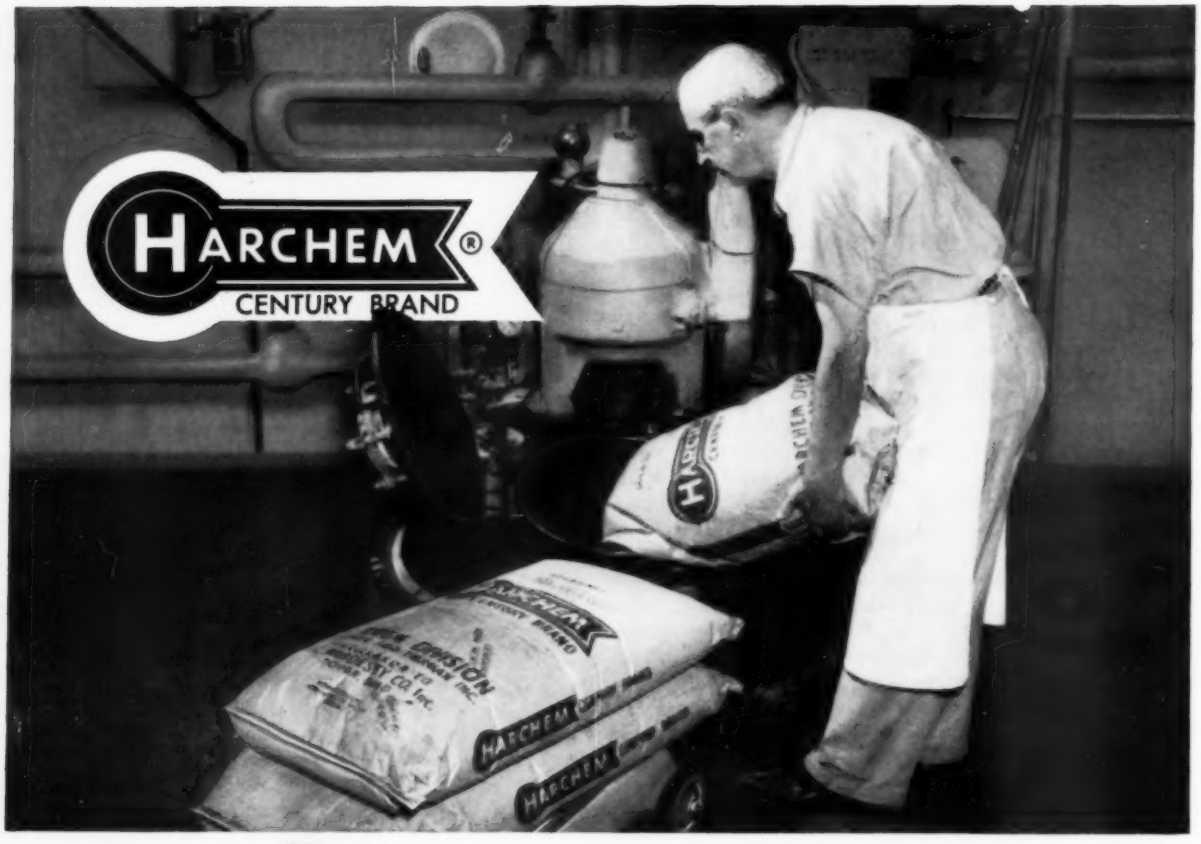
In the first place, the drug company's sole interest in the intermediate is in connection with its use in the synthesis of a therapeutic material. In order to protect the new intermediate, however, the drug company was put in the position of being required to conduct "applications research" in all fields. Quite possibly the novel intermediate could not be shown to be better than the known compound for anything except perhaps as a shoe polish preservative, a field far removed from the drug field. Incidentally, it is not enough to show that the novel intermediate possesses unusual properties not known to have been possessed by the reference compound. It is necessary to show that there is superiority in fact whether the properties of the reference compound are known or not.

Nevertheless, the problem was not too acute because of the time factor. That is to say, since it normally takes two to three years before patent issues are finally resolved and since this period would generally be needed, anyway, to prove or disprove the workability of the overall synthesis, the matter of proving utility of intermediates could be held in abeyance until the answer on the overall synthesis was at hand.

If the synthesis were a failure the whole matter could be dropped. If the synthesis were a success then there was an incentive to go to work on the problem of finding some unexpected superior property of the intermediates. A showing could be made and this would be submitted to the Patent Office in the form of an affidavit. This was accepted as a sufficient showing and the problem was solved as a practical matter, albeit somewhat reluctantly by the drug company.

BUT, this situation did not last long. The Patent Office later came along with a requirement that utility must be stated in the application *as originally filed* in order to be given consideration. In other words, if at the time one files a patent application on a novel intermediate he does not know its unique property over the reference compound which the Patent Office may cite against the application, he is out of luck. It is necessary to state right in the original application that the novel intermediate has this unique property, e. g. as a shoe polish preservative. Then when the reference compound is cited and tested

*Richards and Cifelli
Newark, New Jersey



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and found to be sufficiently inferior to the novel intermediate this information will be sufficient generally to warrant a patent being issued. However, if there is nothing in the original application which refers to shoe polish preservative characteristics in one form or another, then the Patent Office will not give any consideration to such a showing presented during prosecution of the case, as there is no basis in the patent application as filed for such a showing.

That is just about where the situation is today.

Obviously no company in any field can assume the tasks and costs of testing its novel intermediates as against known related compounds to find an unexpected superior use. Such a task is infinitely more difficult than finding the "proverbial needle in the haystack." Even were a company to undertake such a task there is no guarantee that the Patent Office will not rely on some other compound and knock the bottom from the floor as it may well be that this other compound has the same properties as the ones disclosed for the novel intermediate in the application.

What are the practical consequences of this situation?

It is obvious that patent counsel for companies dealing in syntheses involving a number of steps will advise their clients that early publication of the intermediate steps in the syntheses will result in educating the competitors without any protection to the author's company on the intermediates as such. Perhaps process protection may be available but one of the bulwarks of the American drug industry has been the fact that it can obtain product protection in the U. S. A.

Since corporations must necessarily consider the welfare of their business as paramount, a general tightening of the hitherto-liberal policy on publishing pharmaceutical and chemical findings right away appears to be a certainty. That is where the chemist will be hurt. He will be hurt because he may be the one who is not permitted to publish on his findings for a long time, if ever. He will also be hurt because he is deprived of the opportunity of keeping abreast of what is going on in his field; for obviously if the new work of his colleagues is not published, all of the workers in the field are impoverished pro tanto.

Most of all, however, society in general will be hurt because it is too elementary to require proof that society is the greatest gainer from early scientific disclosures; and by the same token it is the greatest loser from the withholding of such information for extended periods. One must not forget in this connection that every disclosure acts as a catalyst to other ideas in the chain reaction of scientific developments.

In other words a scientific Iron Curtain is operating right now in America.

Now, one may ask: if all this is so, why did the Patent Office create such a situation? This question has many sides and no complete answer will be attempted here. If can and should be said at the outset that the various decisions of the Patent Office which have been cited in support of the various propositions which in total have brought about the present situation can be fully justified by the patent laws and previous Patent Office decisions. The men themselves who have made these various decisions are without question staunch believers in the U. S. patent system and its benefits.

The present situation is believed to have arisen primarily from the fact that as each case is decided by the Patent Office its relation to similar cases is the sole criterion. The overall consequences of its decisions do not appear to be generally considered. In other words the approach is to count the trees but not to consider what happens to the forest as a whole.

It is submitted that if the Patent Office were to consider the forest as well as the trees the present situation would not have developed. Specifically, once it became apparent that holdings of the Patent Office in specific cases before it were, when considered with other holdings it had previously made, susceptible to being combined so as to operate against the interests of society in general, the Patent Office might well have raised its sights to rulings or principles which perhaps are of more importance than previous particular decisions of the office.

In this connection it is believed that all it is necessary to do is to go to the U. S. Constitution where in Article 1, Section 8, Clause 8, it is provided:

> The Congress shall have power . . . to promote the progress of science and useful arts, by securing for limiting times to authors and inventors the exclusive right to their respective writings and discoveries.

That is the provision upon which the entire U. S. patent system is based.

What can be done?

1. Of course a simple solution is to refuse to recognize that such a problem exists. This is not as far-fetched as it sounds and particularly so in the patent field where it is often thought that the best way to meet a problem is to deny that it exists. The "flash of genius" doctrine was long handled this way.

2. Legislation is a possible answer to this problem but it is not recommended as it is totally unnecessary.

3. Understanding between the Patent Office and industry is believed to contain the key to the answer. How to effect such understanding has already been considered in these columns. In November 1951, in commenting on a proposal by W. L. Cheesman, of the Northern Regional Research Laboratories, Peoria, Illinois, for a more active technical participation in patent practice, the following general comments were made:

> I believe there is considerable merit to Mr. Cheesman's general proposition, namely, that a scientific organization such as the American Chemical Society should concern itself directly with attempting to effect changes in patent practice. The patent bar is not alone in its interest in the patent system and it does appear to be rather unusual that the patent bar is practically the sole group which thus far has had any active participation in trying to get changes in the patent practice and statutes. In other fields all branches of the industry concerned are usually represented. Thus, one reads in the daily newspapers that the witnesses appearing before the congressional committee considering the status of baseball include not only the legal counsel for the baseball interests, but also active players, both major and minor, owners, managers, etc. While it may be quite complimentary to the patent bar to have full responsibility for espousing the cause of inventors, it can use some help.
>
> Of course, I do not understand Mr. Cheesman to suggest that the patent bar should in any way limit any of its present activities. His suggestion, as I understand it, is that *in addition* to the efforts of the patent bar, technical groups such as the American Chemical Society should concern themselves actively with the problem. The technical people should not pass along their obligation to their patent representatives, as has happened all too

(*Continued on page 96*)

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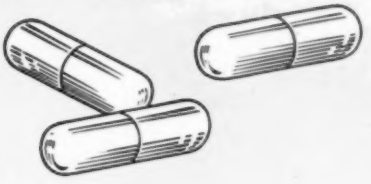

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NEWS . . .

Walker Heads van Ameringen

Charles P. Walker, Jr., formerly executive vice-president of van Ameringen-Haebler, Inc., has been elected president and chief executive officer. He replaces Arnold L. van Ameringen who has become chairman of the board, a newly created post.

Mr. van Ameringen will continue to devote his full time to the interest of the company and states that Mr. Walker's promotion is in line with the firm's policy of continuously strengthening the organization which has increased its sales volume over 50 per cent during the last three years.

A. L. VAN AMERINGEN

Hardt Heads N.P.C.

Robert A. Hardt, vice-president of Hoffmann-La Roche, has been elected president of the National Pharmaceutical Council, succeeding Dr. Theodore G. Klumpp, president of Winthrop Laboratories Inc.

Newell Stewart became executive vice-president. Other officials named were: D. Mead Johnson, Mead Johnson Co.; William L. Arscott, E. R. Squibb & Sons; H. S. Howard, Wyeth Laboratories; and Kenneth Valentine, Pitman-Moore Co. as vice-presidents; L. J. Sichel, Ciba Pharmaceuticals as treasurer; and Wilbur E. Powers, secretary.

Carl K. Raiser, Smith, Kline & French Laboratories, was renamed chairman of the executive committee whose membership includes Arthur C. Emelin, J. B. Roerig & Co.; Nelson M. Gampfer, W. S. Merrell Co.; Paul Gerden, Abbott Laboratories; Leslie D. Harrop, the Upjohn Co.; Dr. Klump; Henry S. McNeil, McNeil Laboratories; F. P. O'Brien, G. D. Searle & Co.; George Orr, Jr., the Ames Co.; and Henry Wendt, Jr., Lederle Laboratories.

Junior Achievement Company

Merck & Co., chemical division, was host on December 8 to six Rahway, N. J., high school students who are officers of Rahmko, Inc., the Junior Achievement company Merck sponsors.

Dr. W. H. McLean, president of Merck's chemical division, greeted William Naiva, president of Rahmko, and five of his staff, discussing the Merck organization.

Rahmko, in line with the national Junior Achievement principle of "learning by doing," produces and sells "Purr," a lanolin-based hand lotion and a TV stool. All members of the Junior company are Rahway High School students who function under the guidance of advisors at the Merck Rahway plant.

CHARLES P. WALKER, JR.

Appointed by Squibb

Arthur E. Tempel has been appointed technical director of the chemical sales department, E. R. Squibb & Sons division, Olin Mathieson Chemical Corp. He will be concerned principally with the company's bulk pharmaceuticals and animal nutrition products.

He has been with Squibb since 1951 when he served as technical assistant to the head of antibiotics manufacturing, and later, as superintendent in charge of fermentation and bulk compounding of antibiotics at New Brunswick, N. J.

Townley Retires—Lakeside

Herbert B. Townley has retired as pharmaceutical salesman for Lakeside Laboratories. Having joined the company in 1935 he covered all of Wisconsin, upper Michigan, Minnesota and much of the Dakotas at that time. Contacting 600 accounts, it took him three months to traverse his territory.

He now plans to devote more time to his hobbies, carpentry and painting.

Durrer on French C of C

E. R. Durrer, president of the Givaudan Corp. and its associate companies, Givaudan-Delawanna, Inc., Givaudan Flavors, Inc., and Sindar Corp., has been elected to the board of directors of the French Chamber of Commerce of the United States Inc.

Heads Chic. Drug Ass'n.

Don H. Coale has been elected president of the Chicago Drug and Chemical Association. Other officers include Glenn H. Reinier, vice-president; Forrest M. Luckett, secretary and William G. Lister, treasurer.

Named as two-year directors were Wallace M. Bruso, Samuel A. Davis, Earl P. Bolen, Alexander B. Moley and David K. Olin. Charles E. Arch was elected director for a one-year term.

DON H. COALE

Darius Honored by Merck

Charles A. Darius was honored last month by the management committee of Merck & Co. on the 65th anniversary of his association with the company. He joined Merck in 1890 three years after the organization was originally founded as a chemical and drug distributing agency in Manhattan.

Since his retirement fifteen years ago as head of the patent law and general legal departments, he has continued to serve the company as a legal and patent advisor.

Dean with Ives-Cameron

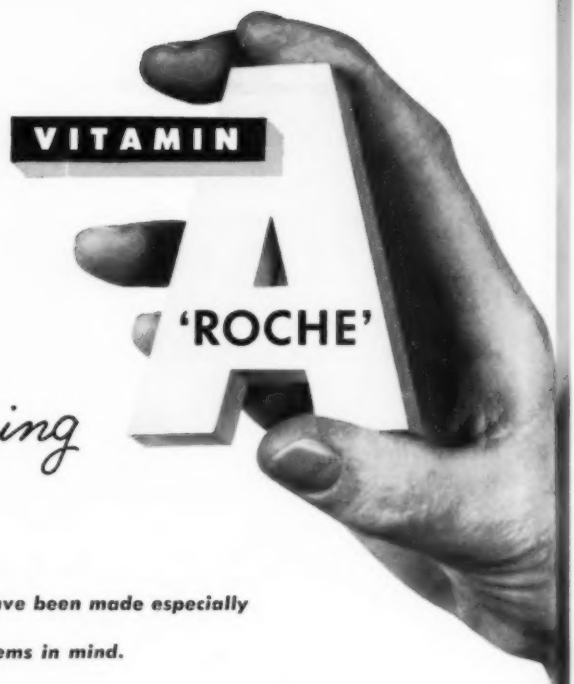
William B. Dean has been appointed director of sales, Ives-Cameron Co., according to Edwin F. Roberts, president. He has been director of veterinary sales for Wyeth Laboratories for the past four years.

Hazleton, Fellow of Academy

Dr. Lloyd W. Hazleton, president of Hazleton Laboratories, Inc., has been elected a Fellow of the New York Academy of Sciences.

Memo to: executives, purchasing agents, technical people

Roche has all popular types of Vitamin A for your pharmaceutical manufacturing



Take your choice of the following types of vitamin A 'Roche'. These have been made especially with your various manufacturing and compounding problems in mind.

LIQUID TYPES

Type P1MO vitamin A palmitate—1,000,000 U.S.P. units per gram, standardized by addition of edible vegetable oil. This type is a highly refined product containing well-proven stabilizing factors of the Roche synthesis. *Experience has shown that this type meets the great majority of pharmaceutical requirements.*

Type P1MO/BHA vitamin A palmitate—Same as Type P1MO above plus the antioxidant-butylated hydroxyanisole (10 mg. per 1,000,000 units of vitamin A).

Type A1MO vitamin A acetate—1,000,000 U.S.P. units per gram, standardized by addition of edible oil. Contains well-proven stabilizing factors of the Roche synthesis.

Type P1.3 vitamin A palmitate—ranging between 1,350,000 and 1,650,000 U.S.P. units per gram. Does not contain any oil addition. Ideally suited for oil-free preparations. Stability is similar to type P1MO.

SPECIAL TYPES

Type P1.8 vitamin A palmitate—1.65 to 1.8 million U.S.P. units per gram.

Type A2.9 vitamin A acetate—2.8 to 2.9 million U.S.P. units per gram.

These special types are available for research and special production in which special handling can be provided.

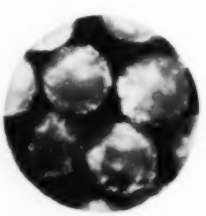
•

Packaging—All liquid types of 'Roche' vitamin A are packed under inert gas in seamless containers. Nominal quantities are shipped in wide-mouth aluminum bottles. For large orders, a specially-designed aluminum transport can holding 50 kilos is recommended. A dispensing attachment is available.

Samples on request; ask your Roche salesman or write Vitamin Division.

DRY TYPES

'Roche' dry vitamin A acetate, and vitamin A and D_3, powders have advantages.



First, extrusion loss is low. This advantage from the product's excellent resistance high pressures found in tablet making.

Second, having an irregular surface the product does not separate from other dry dients during mixing or vibrating.

Third, Roche powders do not stick to machine dies and punches. Capping and spring do not occur during compression.

Fourth, dry vitamin A acetate 'Roche' has high stability in tablets, hard and soft gelatin capsules and powdered food supplements.

The following Roche types have been found most popular:

Type 500-dry vitamin A acetate. 500,000 U.S.P. units per gram.

Type 325-dry vitamin A acetate. 325,000 U.S.P. units per gram.

Type 500 A-50D-dry vitamin A acetate and vitamin D_3. 500,000 U units of vitamin A and 50,000 U.S.P. units of vitamin D_3 per gram

Mesh Sizes: Each type available in two mesh sizes: No. 40 and No

Packaging. All types of 'Roche' dry vitamin A are packed in polyethylene bags, with protective sealer, in drums and in 1 and 2 kilo tamperpruf metal containers. Small quantities in amber screw-cap bottles.

Call **ROCHE** *for Vitamins*

VITAMIN DIVISION • **HOFFMANN-LA ROCHE INC.** • NUTLEY 10, N. J.

NUtley 2-5000 • In New York City dial OXford 5-1400

Pacific Coast distributor: L. H. BUTCHER COMPANY, San Francisco, Los Angeles, Seattle, Portland, Salt Lake City

In Canada: Hoffmann-La Roche Ltd., 286 St. Paul Street, West; Montreal, Quebec

FRITZ DEGENER

Degener with Heyden 25 Years

Fritz Degener, general sales manager of Heyden Chemical Corp., was guest of honor at a luncheon given by Heyden executives in November at the Union League Club, New York. Having completed 25 years with the company, he was presented with a gold watch and diamond service pin by John P. Remensnyder, chairman of the board.

He was a sales representative in the New York office from 1930 to 1935, and in the Chicago office, from 1935 to 1938. Appointed assistant sales manager in 1948, he became general sales manager in 1953.

Meihuizen Visits U.S.

J. E. Meihuizen, managing director of Polak's Frutal Works NV., Amersfoort, Holland, visited the United States during the first half of December and attended conferences at the head offices in Middletown, N. Y.

Cutter Buys Haver-Glover

Cutter Laboratories purchased the assets and business of Haver-Glover Laboratories, Inc., Kansas City, on December 28. The transaction involved cash, and a block of newly issued 4¼ per cent convertible preferred Cutter Stock.

This new acquisition by Cutter, together with its recent purchase of Ashe Lockhart, Inc., establishes the company as an even more important factor in the rapidly expanding national veterinary market.

Dr. Joseph Knappenberger, president of Ashe Lockhart, will also head Haver-Glover as president and director. Clif V. Haver, founder, will remain as a member of the board of directors. Other members of the board will be Ashe Lockhart, D.V.M.; Guy A. Railsback, D.V.M.; Norwood H. Casselberry, D.V.M.; Robert K. Cutter, M.D.; and Harry R. Lange.

Rau, Treasurer, Baxter Labs.

Joseph E. Rau, controller of Baxter Laboratories, has been elected treasurer, according to William B. Graham, president. He has been with the firm 21 years, starting as a production employee.

Wickes V.P., Sterling Drug

Joseph W. Wickes, advertising manager of the Centaur-Caldwell division, Sterling Drug Inc., has been appointed divisional vice-president, according to J. Mark Hiebert, president.

ROLAND J. DAHL

Dahl, Squibb Research Dir.

Roland J. Dahl has been appointed director of research and development of the E. R. Squibb & Sons division of Olin Mathieson Chemical Corp., according to John C. Leppart, executive vice-president. He succeeds Dr. William A. Feirer who has resigned from active duty at his own request and has become a special consultant to the Squibb division in research and development matters.

Named Director of Gair

Hugh C. Laughlin, executive vice-president and a director of Owens-Illinois Glass Co., has been elected a director of the Robert Gair Co., according to George E. Dyke, president. He replaces William E. Levis, a director of Owens-Illinois, who has resigned from the Gair board of directors.

Mid-winter meeting of Scientific Section, Toilet Goods Association, at Waldorf-Astoria Hotel in New York on December 14. Seated on dais, left to right, are Dr. D. H. Powers, Lambert Pharmaceutical Co.; Dr. Herbert Heinrich, Kalmar Research Center; R. L. Patterson, Procter & Gamble Co., Morris J. Root, G. Barr & Co.; Dr. F. J. Austin, Honorary chairman of Section; Dr. Dan Dahle, Bristol-Myers Products division; J. A. Ewald, president, T.G.A., and president of Avon Products, Inc.; Orville Davenport, Avon Products, vice-chairman of Section; H. D. Goulden, T.G.A. scientific director; A. R. Jasuta, Bristol-Myers; Dr. Ivor Cornman, Hazleton Laboratories; and C. L. Bechtold, Colgate-Palmolive Co.

DOW PROPYLENE GLYCOL, U. S. P.

ONE SOLVENT SERVING MANY PHARMACEUTICALS

. . . improving preparations for internal consumption, topical application or injection

The formulation of pharmaceuticals demands a dependable solvent. It must be safe, medically acceptable and a good carrier. Propylene glycol, U. S. P., fills these exacting specifications for many approved pharmaceuticals today—may easily do the same for your products.

In some formulations propylene glycol, U. S. P., also provides important preservative action—others benefit from its emollient, humectant or lubricant properties. Truly versatile in its solvent properties, propylene glycol is effective with many organic chemicals used in the field of chemotherapy—indicating its value in injectables, antiseptics, salves, elixirs and ointments.

Standard of dependability in both quality and supply is Dow propylene glycol, U. S. P. Aiding in product improvement for cosmetics as well as pharmaceuticals, its use has brought economy in many cases. For your sample and information on properties, write to THE DOW CHEMICAL COMPANY, Midland, Michigan, Dept. OC 811 G-4.

you can depend on DOW CHEMICALS

JOHN H. FUNKEY

C. R. HILGENBERG

Leyland with Lakeside Labs.

Dr. Harry M. Leyland, formerly assistant research director of Lloyd Brothers, Cincinnati, has been appointed director of professional service, Lakeside Laboratories. He will be responsible for coordinating the educational activities of the company and providing services and information to the medical profession and pharmacists.

Resign from Coty

Jean R. L. Martin resigned as director of the general research laboratories of Coty Products Corp., on December 13.

Dr. Yolanda Valer, assistant director of the laboratories, resigned at the same time.

Anchor Hocking Elections

John H. Funkey, a vice-president, has been elected president of Carr-Lowrey Glass Co., filling the vacancy created by the recent death of George F. Lang. He was also elected president and a director of Swindell Brothers, Inc.

C. R. Hilgenberg has been elected treasurer of Carr-Lowrey, in addition to his present position of vice-president and secretary.

J. J. Jeffries, vice-president and secretary of Swindell Brothers, Inc., has become assistant treasurer of Swindell.

W. J. Burt, assistant secretary of Carr-Lowrey, has been named assistant treasurer as well.

Cyrus L. Fulton, a director, vice-president in charge of finance for Anchor Hocking Glass Corp., has been elected a director of Carr-Lowrey Glass Co. and a director of Swindell Brothers, Inc.

Fritzsche Sales Conference

Fritzsche Brothers held its annual sales conference from December 5 to 9, with executives, department heads and sales representatives attending. John H. Montgomery, president opened the meeting at the Hotel New Yorker Monday afternoon by presenting Frederick H. Leonhardt, chairman of the board who again welcomed his friends and coworkers to the annual company reunion. He then outlined the plan of the meetings, with the morning sessions devoted to half-hour conferences between each of six executives and department heads and each individual salesman, in addition to visits in small groups to the Clifton, N. J., factory.

He also officially announced the following appointments: R. W. Montgomery, as sales manager; Robert Krone, manager of the flavor division; W. R. Godfrey, manager, perfume division; and E. A. Lawson, manager, industrial odorant division.

J. J. JEFFRIES

W. J. BURT

Keating with Dorothy Gray

Joseph S. Keating has been appointed to the newly-created position of director of sales training and merchandising of Dorothy Gray, Ltd., according to James M. Boohecker, general manager. He was previously national field sales manager, Rockwood Chocolate Co., and prior to that, territory manager of Richard Hudnut Sales Co.

Sales Mgr., Welch, Holme

Irving J. Groeschel has been appointed sales manager of Welch, Holme & Clark Co., according to L. L. Hirsch, president. He has been with the firm 21 years.

Annual cocktail party, buffet supper and dance of Fritzsche Brothers, held December 9 in Crystal and Carnaval Rooms of Sherry-Netherlands Hotel, New York. Nearly 150 visiting sales representatives, executives, and department heads, and their wives, were present.

1923
ANY OIL

1956
PREMIUM OIL

In perfumery too,
you can no longer rely on
just any oils.

Bertrand Frères is a prime source
for the finest
floral and essential oils.

Bertrand Frères, Inc.

443 FOURTH AVENUE NEW YORK 16, NEW YORK

FRANCE: Grasse, Avenue Font-Laugiere
Paris, 12 Rue Leon Jost

ENGLAND: London, 1 Crutched Friars

ADCIOM Elections

Joseph W. Wise, Grove Laboratories, was elected president of the Associated Drug and Chemical Industries of Missouri at the annual Christmas party on December 14 in the Hotel Chase. Additional officers elected were A. L. Saeks, the Puro Company, as first vice-president; E. Ted Mann, the Dow Chemical Company, second vice-president; Leo G. Peck, Peck's Products Company, third vice-president; S. C. Gansner, Cole Chemical Company, secretary; and J. Louis Lanz, consultant and manufacturer's agent, treasurer.

Members of the executive committee are Robertson B. Clark, Mallinckrodt Chemical Works; I. W. Kurtz, Jr., the Blue Line Chemical Co.; Dr. George F. Reddish, Lambert Pharmacal Co.; G. Kenneth Robins, G. S. Robins & Co.; W. D. Vesey, Merck & Co.; and Robert F. Walsh, Harry A. Baumstark & Co.

Egan with Amer. Alcolac

Richard R. Egan has joined American Alcolac Corp. as head of its commercial research activities. He will be responsible for the development of new or improved surfactants and derivatives of fatty alcohols and related new products. He will also be in charge of quality control.

Owens-Ill. Glass Appointments

J. J. Geagan, supervisor of field representatives, has been appointed assistant manager of the prescription ware division, Owens-Illinois Glass Co., according to Sidney F. Davis, vice-president and division general sales manager.

Roy G. Burton, central district manager, has been promoted to field manager, retail sales, and Robert A. Dube, a glass container salesman in the Chicago branch, has become field manager for wholesales sales.

J. J. GEAGAN

Attending Givaudan-Delawanna annual Fall reception and cocktail party on November 17, left to right: Frazer V. Sinclair, Beauty Fashion; H. Gregory Thomas, Chanel Inc.; E. R. Durrer, president of Givaudan; R. K. Miffen, Lentheric; and Benson Storfer, Parfums Corday.

Trubek Buys Truland Chem.

Trubek Laboratories has acquired Truland Chemical Co. of Union, N.J., which will become a wholly-owned subsidiary with no change in personnel.

Dr. Daniel Friedland and Dr. Edward Trueger, co-founders of Truland, will be retained as vice-presidents of Truland Chemical Co., division of Trubek Laboratories.

The operations of Truland, which include the custom reclamation or purchase of organic chemical by-products, will be moved to East Rutherford.

Anderson, Secretary of Merck

Carl M. Anderson has been elected secretary of Merck & Co., effective February 1, according to John T. Connor, president. In addition to being secretary of the board of directors and of the executive committee of the board, he will have certain other executive responsibilities.

He joined Merck in 1934 as head of the legal department and since then has held several administrative posts including, most recently, that of vice-president of the Merck-Sharp & Dohme International division.

CARL M. ANDERSON

Heyden Expands in Mexico

Heyden Chemical Corp. has acquired a one-third interest in Salacilatos de Mexico, Mexico City. This firm recently installed Mexico's first salicylic acid plant with a capacity said to be sufficient to supply Mexico's requirements and produce a surplus for export.

Two-thirds of the stock of Salicilatos de Mexico is owned by Meixcan investors. The company also has a Mexico City aspirin plant.

Simon Askin, Heyden president, and James K. Lindsay, secretary, have been elected directors of the Mexican firm.

Promoted by Sterling Drug

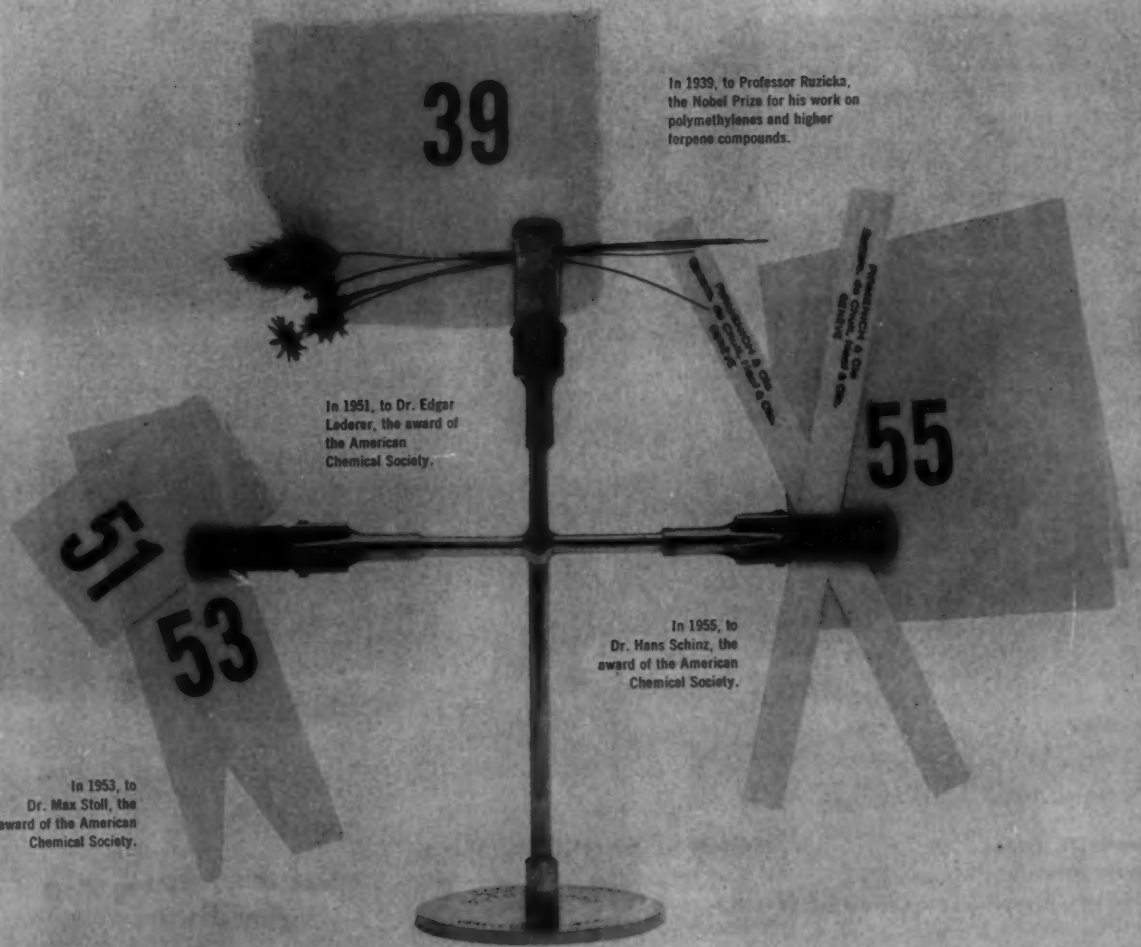
A. J. Burns has been elected vice-president in charge of sales, Sterling Drug Inc., and J. N. Cooke has become vice-president in charge of marketing and sales promotion. Mr. Burns had previously been divisional vice-president of the Chas. H. Phillips Co., a Sterling division. Mr. Cooke had been director of marketing for Sterling.

D&O Moves Chicago Office

Dodge & Olcott has moved its Chicago sales office to 5537 North Clark Street, Chicago 40. The office is under the direction of Kenneth Hartley. Telephone number is Longbeach 1-8996.

Heads N.Y. Cos. Chemists

William Lambert, Editor of *American Perfumer and Aromatics*, has been elected chairman for the coming year of the New York chapter of Cosmetic Chemists. Warren B. Dennis, Shulton, Inc., is chairman elect; Beverley Meigs, a sistant director of research, Colgate-Palmolive Co., is secretary; and Theodore Ostrowski, Germaine Monteil, has become treasurer.


39
In 1939, to Professor Ruzicka, the Nobel Prize for his work on polymethylenes and higher terpene compounds.
In 1951, to Dr. Edgar Lederer, the award of the American Chemical Society.
55
51
53
In 1955, to Dr. Hans Schinz, the award of the American Chemical Society.
In 1953, to Dr. Max Stoll, the award of the American Chemical Society.

an award . . . an award . . . an award
and now another award
to a member of the research staff
of Firmenich

The harmonious coordination of industrial and scientific research, originally established by M. Philippe Chuit and Professor Ruzicka and carried forward by Dr. Max Stoll and his associates, has borne much fine fruit in the field of organic synthetics for perfumes and flavors. So these distinguished citations—the Nobel Prize and the awards of the American Chemical Society under the Fritzsche grant—bear witness. So does the increasing preference for Firmenich products as it is expressed by customers throughout the world.

FIRMENICH & CIE
CHUIT, NAEF & CIE

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VICTOR E. WILLIAMS

With Monsanto 40 Yrs.

Victor E. Williams, regional vice-president of Monsanto Chemical Co. in New York, completed 40 years of service with the company on December 13. He has spent 30 of these years in New York, where he is now the ranking eastern representative of the firm's organic chemicals division.

He joined Monsanto in 1915 as an office boy and by 1925 had become office manager of the New York office. In 1943 he was appointed director of sales for the organic chemicals division and was named a regional vice-president in January, 1954.

Named by SKF Inter-American

Robert J. Byrnes, formerly production and engineering section head of Smith, Kline & French Inter-American Corp., has been appointed director of manufacturing at the Canadian branch of the company.

J. T. Baker Expansion

J. T. Baker Chemical Co. has completed additional unit process facilities for manufacturing purified and reagent chemicals in tonnage quantities. The entire operation is engineered to protect against accidental chemical contamination or extraneous matter of any kind. A stainless steel blender with a capacity up to 10,000 pounds is part of the complete operation. Final blending of the material provides a homogeneous lot and assures that the sampling and analysis is representative.

Some of the Baker purity chemicals that will be made in these new facilities are aluminum nitrate, ammonium chloride, ammonium phosphate, barium acetate, barium chloride, barium hydroxide, magnesium chloride, silicic acid, sodium sulfate, strontium hydroxide, and zinc acetate.

Luis de Hoyos, left, vice-president, Synfleur Scientific Laboratories, being congratulated by Jack Ardis, award chairman, on trophy he received for winning the 1955 Angling Championship of the Miami Beach Rod and Reel Club. He was also awarded another trophy for the outstanding individual catch of the year, by a club member—an 80-pound Pacific Sailfish taken on regulation fresh-water plug casting tackle.

Pfizer Appointments

Carl E. Lotz has been appointed manager, and Daniel Minicucci, sales service manager, of the Metropolitan New York region, Chas. Pfizer & Co. John F. Zea has become manager of the Northeastern region.

Additional appointments include Harold Krauss, district manager of the New York City district; William O' Connell, district manager, Boston district; Edward de Vincentis, sales service manager, Northeastern region; and Harry Chorpenning, manager of the Des Moines, Iowa, district.

Patton in Lentheric Post

Wiley F. Patton has been appointed assistant to the director of marketing of the Lentheric division of Olin Mathieson Chemical Corp., according to Jack H. Mohr, general manager of the division. He was formerly associated with Hudnut Sales Co. for over 10 years.

WILLIAM T. DOYLE

Nordmark Expansion

Nordmark Chemical Co. has formed a new company, Nordmark Pharmaceutical Laboratories, Inc., at 35-A Ellis Ave., Irvington, N.J. The original firm was established in New York in 1931 as a bulk chemical supplier to the pharmaceutical industry.

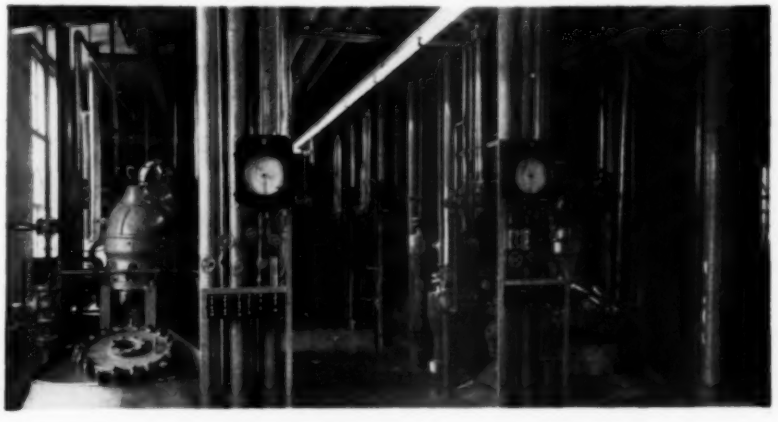
In this new move the company has expanded its operations and will now have a bulk chemical division to serve the industry, and a pharmaceutical specialty operation to serve the medical profession.

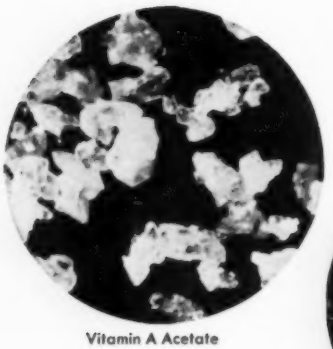
William T. Doyle has been elected president and James F. Bush, Jr., vice-president, in charge of sales of both operations.

Fritzsche Moves Boston Office

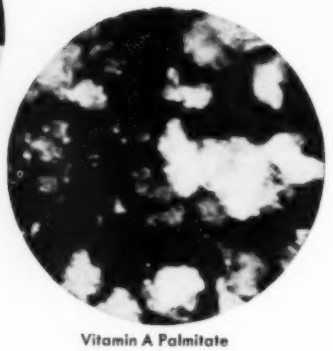
Fritzsche Brothers has moved its mid-town Boston office from the Statler Building to 661 Washington St., Norwood, Mass. The telephone number is NOrwood 7-3303. The increasing shift of industry away from congested metropolitan locations to more accessible suburban areas was a major consideration in the company's decision.

J. T. Baker Chemical Co.'s new unit process facilities for manufacturing purified and reagent chemicals in tonnage quantities. The operation is for the protection against accidental chemical contamination or any kind of extraneous matter, with the final blending providing a uniform batch.





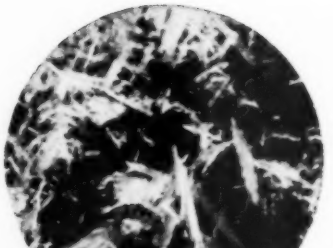
Vitamin A Acetate



Vitamin A Palmitate

Some **vitamin A** we sell

Oil solutions of vitamin A acetate and vitamin A palmitate, sold under the trademark "Myvax" to the pharmaceutical and food industries, are what keep the wheels turning for us.



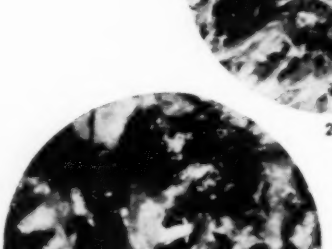
2-cis-Vitamin A

and some we just study

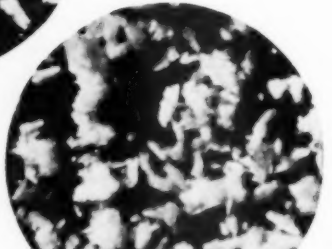
These forms of vitamin A we have made, not for money but for curiosity. All we have made of them has been used up in various experiments. However, if some chemist wants some, we will happily send him a collection of six reprints from the *Journal of the American Chemical Society*. From the papers he ought to be able to figure out how to twist vitamin A for himself into these odd geometrical isomers.

Frankly, we did not know in advance how valuable something like 2,6-di-cis-vitamin A would be. The main reason we made it was that as long as we want to be leaders in research and production of vitamin A, we couldn't very well afford not to, once the idea occurred to us. Even if for no other reason than to make sure there was none of it in our product.

That's our attitude toward vitamin A. If you would like to do business with us, write ***Distillation Products Industries,*** Rochester 3, N. Y. Sales offices: New York, Chicago, and Memphis • W. M. Gillies and Company, Los Angeles, Portland, and San Francisco • Charles Albert Smith Limited, Montreal and Toronto.



6-cis-Vitamin A



2,6-di-cis-Vitamin A

leaders in research and production of vitamins A and E

DPi

Also . . . distilled monoglycerides . . . some 3500 Eastman Organic Chemicals for science and industry

All illustrations are 15× photomicrographs of crystals of the various vitamin A esters and isomers.

Distillation Products Industries *is a division of* **Eastman Kodak Company**

ROBERT G. URBAN

Urban, Exec. V.P., Lambert

Robert G. Urban has been appointed executive vice-president of the Lambert-Hudson division of the Warner-Lambert Pharmaceutical Co., according to Alfred E. Driscoll, Warner-Lambert president. He will be responsible for the marketing activities of the division, including sales, advertising, merchandising and product development, as well as sales planning and budgetary control. Mr. Urban was formerly vice-president and director of marketing of the J. Walter Thompson Co.

In the future, all research, manufacturing, marketing and financial functions of Warner-Lambert's toiletry and cosmetic businesses will come under the Lambert-Hudnut division.

Johnson in Corday Exec. Post

Harry T. Johnson has been appointed to the newly created position of general sales manager, Parfums Corday, Inc., according to Herbert F. Storfer, executive vice-president. He had previously been general manager of Elizabeth Arden, and general sales manager of Helena Rubinstein and Kathleen Mary Quinlan.

Warner-Lambert Plant, Cuba

Warner-Lambert, S.A., the Cuban affiliate of Warner-Lambert Pharmaceutical Co., opened its new $250,000 plant in Havana on December 16. Company executives, including Elmer H. Bobst, chairman of the board, Warner-Lambert, and Alfred E. Driscoll, president, participated, as well as church dignitaries and high Cuban government and Embassy officials.

Warner-Lambert, S.A. manufactures a wide variety of ethical pharmaceuticals, proprietary drugs, toiletries and cosmetics. General manager of the firm is V. A. Eigenmann.

Pete Niles, manager of Fritzsche Brothers' Chicago office, at his desk with congratulatory telegrams, marking his 25th anniversary with the company.

Niles with Fritzsche 25 Yrs.

Pete Niles, Chicago manager of Fritzsche Brothers, Inc., became the 50th active member of Fritzsche Brother's Quarter-of-a-Century Club on December 1 when he was honored by the entire Chicago staff at a banquet at the Drake Hotel.

SAACI Nominations

The nominating committee of the Salesmen's Association of the American Chemical Industry has proposed the following members for the 1956 officers: E. L. Collins, Chilean Nitrate Sales Corp., as president; Vincent L. Rebak, Grace Chemical Co., vice-president; Robert J. Roberts, Emery Industries, Inc., treasurer; and James E. Spencer, Harshaw Chemical Co., secretary.

Proposed for the board of directors were Joseph R. Augello, J. T. Baker Chemical Co.; Charles E. Griffith, R. W. Greeff & Co.; Lester Johnson, International Nickel Co.; W. Gilbert Kayser, Jr., Sharples Chemicals, Inc.; and Herman M. Schulman, Washine National Sands, Inc.

Nacca, Exec. V.P., Organon

Raphael M. Nacca, vice-president in charge of marketing, Organon Inc., has become executive vice-president, and a director, of the company. He has been with the company in various promotional and marketing positions since 1940 and became a vice-president in 1951.

HERMAN W. LEITZOW

Leitzow, V.P., Schering

Herman W. Leitzow has been promoted to vice-president of Schering Corp., according to Francis C. Brown, president. With Schering 14 years, he has been domestic sales manager for the past ten.

Mead Johnson Appointments

Harold O. McCutchan, formerly vice-president, finance, and treasurer, has been elected executive vice-president of Mead Johnson & Co. Edward F. Hassee, formerly assistant treasurer, has become treasurer.

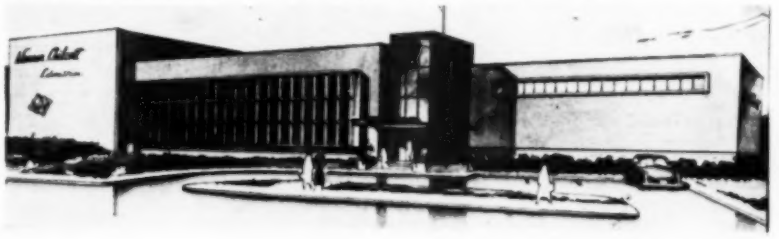
Lambert D. Johnson, Jr., vice-president for advertising and promotion, has been named vice-president and general manager of the newly created Mead Johnson International division.

Werner R. Voigt has been appointed vice-president for operations of this new division which will be responsible for all of the firm's overseas operations.

Gerald L. Long has been promoted to director of advertising and promotion, having previously been advertising manager. He will be responsible for all advertising, sales promotion, and package design, succeeding Mr. Johnson in that capacity.

Mr. Johnson is a grandson of the founder of the company, and the son of the late Lambert D. Johnson, Sr., former president and chairman of the board.

Architect's drawing of new $250,000 plant of Warner-Lambert, S. A., Cuban affiliate of Warner-Lambert Pharmceutical Co. It was officially opened in Havana on December 16.



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We are pleased to announce that hexachlorophene and hexachlorophene liquid soap have been included in the fifteenth revision of the Pharmacopoeia of the United States.

As the discoverer and producer of hexachlorophene, we welcome this further recognition by the medical profession and the privilege of joining the U.S.P. list of best-known and most important medical aids.

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McCabe Appointed by Merck

James E. McCabe, secretary of Merck & Co., has been appointed director of market planning of the chemical division, effective February 1, according to Thomas J. Treacy, director of sales and marketing. He will be responsible for product merchandising, technical customer service, and sales analysis, as well as market planning and development.

He will succeed Dr. Frank M. Parker who has resigned.

New Plant in Venezuela

Fred Capriles, president of Industrias Farmaceuticas Associadas C.A., Caracas, Venezuela, has set up a new plant for the manufacture and distribution of pharmaceuticals and cosmetics. He states he is in a position to manufacture products for American firms under license and under their own private brand and is ready to cover the entire line in the pharmaceutical and cosmetic field. He suggests that any firm which might have difficulty in shipping into Venezuela because of high import duties can make use of these facilities in order to enter the Venezuelan market.

Any one interested in further information may contact Mr. Capriles at Apartado 2277, Caracas, Venezuela.

Lever Promotions

Leonard D. Dunlap, formerly eastern regional sales manager for the Pepsodent division of Lever Brothers Co., has been promoted to the newly created post of field sales manager, according to V. T. Finch, sales manager.

Bennett with Squibb Institute

Dr. Ralph E. Bennett has been appointed head of the microbial biochemistry laboratories at the Squibb Institute for Medical Research, New Brunswick, N.J.

Appointed by Nat. Aniline

Roland F. Willenbucher has been appointed manager of purchases and traffic, according to M. A. Conner, vice-president of National Aniline division, Allied Chemical & Dye Corp.

Taylor with White Laboratories

Dr. Richard M. Taylor has been appointed director of the pharmacology laboratory, according to Dr. Edward R. Neary, medical director, White Laboratories. He was formerly on the research staff of the Upjohn Co.

MORRELL NUNN

Nunn with Strong Cobb

Morrell Nunn has been appointed assistant to the president, Strong Cobb & Co., according to Eustis, president. He had formerly been in the marketing division of Merck & Co.

He will be responsible for coordinating Strong Cobb services with customer needs and also for carrying out management responsibilities.

Hooker Named SOCMA Pres.

T. Wolcott Hooker, vice-president of Hooker Electrochemical Co., was elected president of the Synthetic Organic Chemical Manufacturers Association at its 34th annual meeting in New York last month. He succeeds Dr. Samuel Lenher, vice-president, E. I. du Pont de Nemours & Co.

Named Director, State Pharm.

Dr. Joseph Schultz, president and board member of Lanolin Plus, Inc., has been named to the board of directors of the State Pharmacal Co., according to Jack Mathis, president.

Penick Sets Up Fellowship

S. B. Penick & Co. has established a graduate fellowship in organic chemistry, particularly in the field of alkaloid chemistry, at the University of Wisconsin for the year 1955-1956. The University is in Madison, Wis.

Roe S. Clark

Roe S. Clark, president of the Package Machinery Co. since February, 1952, died at his home in Springfield on December 22. He was also chairman of the board of the Reed-Prentice Corp., Worcester, a wholly owned subsidiary. He has been associated with the company since 1916 when he started as a factory accountant, becoming assistant treasurer in 1921 and treasurer in 1931.

John C. Isdahl

John C. Isdahl, president of Isdahl & Co., A.S., Bergen, Norway, died November 26 of a heart attack. He was a former director and officer of McKesson & Robbins. Isdahl & Co. was one of the pioneers of cod liver oil.

Ernest Cohn

Ernest Cohn, advertising manager of Pitman-Moore Co., died November 29 in Robert Long Hospital, Indianapolis. He was 71 years old and had planned to retire December 1 after 38 years with the firm and more than 50 years in the advertising field.

He was a recognized authority on medical superstitions. Part of his collection of material on the subject is on exhibit in the Smithsonian Institute in Washington, D.C., and the Museum of Man in San Diego, Calif.

Mr. Cohn is survived by his widow, Mrs. Rose L. Cohn; a daughter, Mrs. Herschell Goodman; a son, Dr. W. L. Cohn; and two grandchildren.

P. Val. Kolb

P. Val. Kolb, 70, president of Sterwin Chemicals, Inc., died December 5 at Rock Hill, South Carolina. He had been with Sterwin since 1940 and at his death was also president of Sterwin Chemicals of Canada, Ltd.

He started his business career with the Tennessee Coal and Iron Works and later joined Swan Chemical Co. This company acquired Provident Chemical Works, of which Mr. Kolb was named president in 1931. He joined the American Agricultural Chemical Co. until 1940 when he became associated with Sterwin.

He is survived by a sister, Mrs. W. J. Roddey, Jr.; two nieces, Mrs. Kenneth Donnalley and Ann Roddey; and two nephews, Peter V. and Albert W. Metcalf.

George F. Lang

George F. Lang, president of the Carr-Lowrey Glass Co. and a director of the Anchor-Hocking Glass Corp., died November 30 at his home in Baltimore after a month's illness. He was 71 years old. He was also president of Swindell Brothers, Inc., a wholly-owned subsidiary of Carr-Lowrey, and president of Glass Crafters, Inc., a partially-owned subsidiary.

Mr. Lang was a national figure in the glass industry and a founder and first president of the Glass Container Manufacturers Institute.

Meet the Newest in Precision Tabletting

Simplified set-up and adjustment

Economy of operation

Improved controls and safety features

High production rating

...All with the new Stokes rotary tablet machines

The most advanced design ideas, based on over fifty years of Stokes experience in the Pharmaceutical field, have been built into the new Stokes rotaries.

Compare them for ease of set-up, adjustment and operation. New centralized controls at front of press—new push button hydraulic pressure adjustment of upper roll is faster, more accurate.

Compare them for economy of operation. Lower maintenance, power and labor costs—less floor space.

Compare them for improved controls and safety features. New direct reading dial indicators—new centralized pressure lubrication—greater overload protection.

Compare them for production rating. 10-ton and 4-ton machines conservatively rated at 900-2500 and 950-2700 TPM respectively. High speed if you need it with no compromise in product quality.

Write for Bulletin No. 650. F. J. Stokes Machine Company, 5502 Tabor Road, Philadelphia 20, Pa.

STOKES

Management Forum

by Francis Chilson

INDUSTRIAL CONSULTANT

Company Conferences

Happy New Year! We'll start the new year off with a discussion of company conferences. Quoted below is a somewhat lengthy discussion on the subject of conferences which I pinched from a recent issue of Time. (It looks as if the editor had been reading my articles over the past several years.)

"Once upon a time, so the story goes, a businessman had a nightmare. He was forced to watch helplessly while production was slowly strangled because of company conferences. Everyone, from vice presidents to foremen, was so busy conferring that no one had time to do any work. When the businessman awoke, he found the nightmare was real. His company was indeed paralyzed by too many conferences. His solution: a conference to do something about conferences.

"As U.S. business has grown bigger and more complex, it has become increasingly hard for executives to make decisions individually; more and more they tend to rely on conferences. Now many businessmen wonder whether management-by-conference has not been carried too far. Says a New York executive: "They keep you so busy 'familiarizing' you with the 'problems of the other fellow' that you don't have time to solve your own." A manager of a big Eastern manufacturing plant guesses that he spends 65 per cent of his time in conferences. How much of it is usefully spent? Says he bitterly: 'None.'

"Despite all the jeering and complaints, most businessmen agree that in a complex, highly diversified company, conferences are essential. Says Board Chairman Frederick C. Crawford of Thompson Products, Inc.: 'Companies that have decentralized, as we have, have run into the problem of communications between divisions. Conferences have become increasingly important to us.' Says Boeing Airplane Co.'s Senior Vice President Wellwood E. Beall: conferences can be 'good for morale and give an increased sense of participation in policymaking.' Furthermore, decisions made by a group in which everyone understands the "why" of the decision have a better chance of being carried out as intended.

"But one big danger is that conferences will be used, not to reach decisions, but to put them off. When a man runs up against a sticky problem there is always the temptation for him to appoint a committee or call a conference to get him off the hook. A variation of the decision-postponing conference is the loaded conference. This is called after an executive has already buttonholed the conferees, thus assured himself that they are in agreement with him. Then a time-wasting formal conference is called, simply to hedge the executive against criticism should his decision later turn out to be wrong.

"Other conference faults are poor preparation and direction. Often a group meets before anyone has studied the subject, and the discussion is allowed to wander.

"To avoid these pitfalls, some companies have adopted what is virtually a conference manager. Standard Oil Co. of California, for example, got worried about the problem about twelve years ago, and put Conference Organizer Lewis Purkey to work on it. Says Purkey: 'It took me and my staff three weeks just to find out how many committees we had and what they were supposed to do. We found that we had about 200.' Purkey set up stringent rules governing the forming of committees and running of conferences. Now every new committee must have a written outline stating its purposes before it can be formed and must convince Purkey that the purposes are worthwhile. When a committee's useful life is ended, it must disband. Discussions at meetings are held closely to the problem. Furthermore, only the board of directors and the executive committee have authority to make group decisions; every other conference group reports to an individual executive, and he alone makes decisions and takes the responsibility. As a result of Purkey's pruning, Standard's committee count is now down to 57.

The NEW Installations are COLTON

CIBA REPORTS OVER 3,000,000 TABLETS PER DAY

Mr. James Beattie, Public Relations Director of CIBA reports upon the performance of their Colton Tableting Equipment as follows:

"Faced with ever-increasing demand for Ciba's SERPASIL, we turned to Colton and their Model No. 241*. Since purchasing our first unit over 18 months ago, we have added two more units to increase our production to over three million tablets per 8 hour day on the three units."

*Colton No. 241 Rotary Tablet Press

Colton is the only complete line of modern tableting equipment. It includes everything for high-quality, low-cost production at capacities up to over a million a day per machine. Your inquiries are invited.

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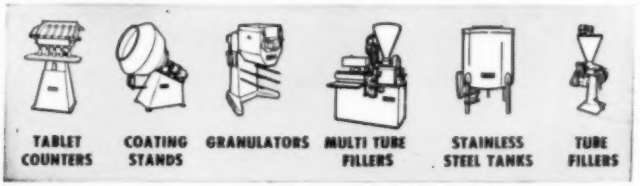


"Pacific Gas & Electric Co. prefers more informality. It lets conferences ramble a little, on the theory that this gets minds working and ideas flowing. Says Executive Engineer James Moulton: 'There are a lot of things that an executive doesn't want to put down in writing. A man will often say things that may not be sound or serious just to stimulate someone else.' But like Standard, P.G.&E. puts the job of making decisions squarely on the shoulders of individual executives.

"While there are still executives who yearn for the old days, when the boss gave orders and everyone else carried them out, there is no doubt that conferences are likely to become even more solidly established as a handy management tool—if wisely used."

New 4-Ton High Speed Rotary Tablet Machine

Another new high speed rotary tablet machine, Model 540, with a maximum operating pressure of four tons and with production ratings ranging up to 3000 tablets per minute and capable of even higher output, has been added to its line of automatic pharmaceutical machinery by F. J. Stokes Machine Company, Philadelphia, Pa.

Like the same company's Model 533 10-ton press announced just a month ago, the new Stokes Model 540 press is a completely new machine, whose design reflects Stokes' continuing study of the increasingly exacting requirements of the pharmaceutical industry.

The new Stokes Model 540 press has 41 stations, and can make tablets up to a maximum diameter of 7/16 inch and 11/16 inch depth of fill at rates from 1000 to 3000 per minute.

Tablet production at rates higher than those cited has already been attained in field trials of the new machine, in circumstances where material consistency, depth of fill, and other factors offered the optimum in operating conditions.

The new Stokes press incorporates a number of exclusive advanced design features which make for greater flexibility of adjustment of operating conditions, easier and more precise control, and greater economy of maintenance.

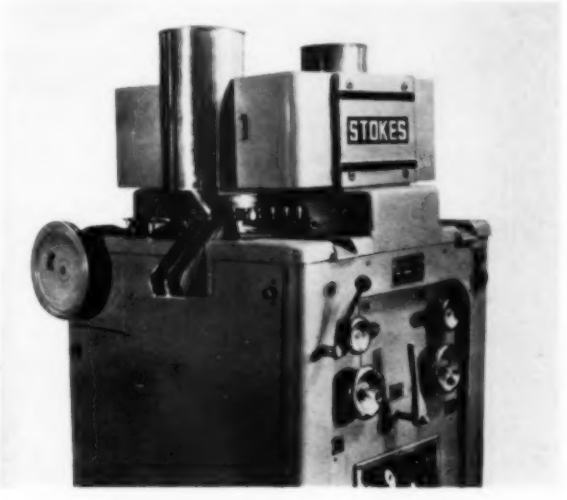
Hydraulic loading of the upper pressure roll replaces the ratchet spring loading used on older types of presses, and makes possible faster, more precise adjustment of the pressure exerted by the machine, thus more accurate control over the density of the finished tablet. This simple type of adjustment permits changing the entrance of the upper punch and altering the compacting pressure with a single push-button type of control.

"Non-drop" inserts in the lower pressure roll prevent double impressions occurring in the production of embossed tablets. Regardless of the roll setting, these inserts prevent the punch from jumping off the tablet until the moment of ejection.

"Anti-jump" retainers on the lower cams prevent damage to the punch or die when the machine runs low on powder.

Individual die screws, one to each die, make it easier and quicker to set up odd punch and die shapes. This construction makes the die table stronger than the older type of arrangement with one screw to every two dies.

A large diameter punch circle and wide roll faces reduce the load on bearing surfaces and punches, thus providing a generous safety margin for high speed operation as well as ample overload protection. The new Stokes rotary press has the lowest roll pressure rate—12,450 lbs. per inch of displacement—of any



rotary tablet machine ever offered, the manufacturer states. This low pressure rate means greater protection for delicate tooling and longer life for moving parts.

Neckless punches can be used on the new press. These punches provide much greater strength and rigidity to the tooling, and result in longer punch life and therefore lower tool cost per tablet.

All controls are grouped at the front of the press, where they are easily accessible to the operator, so that changes in tabletting procedure can be made even while the machine is running. This is a big help toward simpler, fool-proof operation.

New, direct-reading dial-type tachometers, which indicate production directly in tablets per minute, and pressure indicators, graduated in tons, are grouped with the other controls at the front of the press. The pressure indicator not only assists in accurate adjustment of the press but makes it easy to record the pressures found best for making each particular tablet. It incorporates a safety switch, too, to prevent overloading of the press.

Feed frames for both fill stations can be clearly seen from the control position at the front of the press. This facilitates quick and accurate adjustment of the depth of fill.

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LIQUID FILLING REQUIREMENT

and profit by more than two generations of liquid filling experience. The U.S. line covers a wide range of liquid filling machines for automatic, semi-automatic and hand-filling operations. With this wide choice of Fillers, you need not compromise your production to fit a machine; instead, basic U.S. machines are custom-engineered to fit your specific production . . . and usually at a saving.

Model B-2 Vacuum Filler

provides efficient continuous production, filling two containers at a time. Handles a wide variety of liquids and semi-liquids. Has automatic product supply; vacuum is adjustable and flow regulated for accurate, clean filling. Fills a wide range of containers up to 4⅛" dia. round or rectangular. Send for Bulletin B-2.

The U.S. Siphon Filler

is a highly efficient machine. Stainless steel filling tubes and glass lined tank. Handles all types liquids; all containers. Fills without overflow or spillage. Send for Siphon Bulletin.

Model B-49 Straightline Vacuum Filler

for liquids and semi-liquids. Most automatic one-operator multiple filler. Operates with or without discharge conveyor. Filling proceeds automatically while empties are loaded. Easy operating lever activates container feed and discharge; otherwise operation is completely automatic. Adjustable for container sizes from AGST to gallon size finishes. A dependable machine where filling cost is a factor. For full details, send for Bulletin B-49.

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All manual adjustments are made by handwheel from the operator's normal location.

Automatic, gear-operated lubrication of the new Stokes rotary press is another new feature, offered for the first time in this field. This centralized lubrication system provides oil under pressure to all vital points in the machine where wear could occur. A replaceable-cartridge oil-filter and a heavy-duty gear pump in the oil system insure positive, trouble-free lubrication at all times.

Compact design makes the new Stokes machine the lowest in floor-space requirements of any rotary machine on the market.

Styling of the new Stokes press is modern, handsome, and functional. Panels and aprons are completely removable for greater accessibility when cleaning or other servicing is required. Improved dust protection for moving parts is provided by sealed drive units and sealed upper punch guards.

Other features which contribute to the efficiency and economy of the new Stokes rotary press are:

1. Stainless steel hoppers provide smooth powder flow; are easily removable for cleaning.
2. Feed frames are supported at three points to permit transit-type leveling for better material economy.
3. Multiple dust nozzles provide cleaner operation. Common discharge collects all powder at one disposal point.
4. Vibration mounting eliminates need for foundation or attachment to floor and permits leveling of entire machine.
5. Totally-enclosed variable-speed drive is designed for long life with hardened worm gear and replaceable bronze gear ring in head.
6. Heavy-duty clutch is accessible on worm shaft; is connected through linkage to low-effort lever on control panel.
7. Heavy-duty ball, needle and roller bearings are used at vital points.
8. Hardened replaceable inserts protect adjustment points from wear.
9. Upper cams support punches at all times.
10. Removable upper dwell cam permits set-up of odd punch shapes.
11. Upper and lower punch lubricators are provided.
12. When desired, a tablet thickness calibration can be provided.

Dumpit

The following explanation will enable you to select exactly the right DUMPIT model for your dumping drums, barrels, bins etc. with any conventional fork lift truck.

The top hook of the Standard DUMPIT slides free on the mast in vertical position. It automatically locks in place when dumping. To pick up the drum which is to be dumped, lower the DUMPIT against

the side of the drum, catching the top edge of the drum in the top hook. Continue lowering until the bottom hook is just clear of the ground.

Driving the fork truck forward tilts the drum slightly, and permits the bottom hook to pass underneath. Lifting the DUMPIT then engages the drum, top and bottom, with the weight of the filled drum resting on the rigid bottom hook. Pull the hand line from any position, and the drum will rotate forward, pouring out the contents.

The emptied drum may be returned to vertical by lowering against the side of the receiving vessel, or to the ground and backing the fork truck while continuing to lower. Disengaging the drum is the reverse of the engaging procedure.

With very little practice it will not be necessary for the fork truck operator to leave his seat from pickup to release.

For operation on "slick" floors it will be necessary to push the drum against some non-slip obstruction at the bottom in order to tilt it forward for pickup. The same results may be accomplished by painting the pick-up area with an anti-skid paint.

For those fork trucks whose forks swing free on a rod it will help the operation to f sten one fork back against the plate. An ordinary "C" clamp will do, or any other positive f stening.

The EXTRA for plain bottom containers includes: (1) a flat pan which fits over the bottom hook, and onto which the container is manually "walked," and a chain hook, which is part of the pan. This is a particularly useful arrangement for dumping materials received in fibre drums. The unit may be quickly converted to a regular DUMPIT by simply removing the bottom pan.

The "HEAVY" of the DUMPIT family will handle tote boxes weighing up to one ton gross. It has three books which automatically lock when dumping to prevent dropping the box. The tote boxes must have lugs fustened to top and bottom to receive the hooks of the DUMPIT. The Heavy is custom built for specific needs.

Any drum becomes a scoop when held horizontal on the DUMPIT, but where volume requires a better tool, a DUMPiT SCOOP bucket can be supplied which is quickly interchangeable with the DUMPIT mast.

DUMPIT is made by Basic Methods Inc., 18 Barnsdale Road, Short Hills, N. J.

New Tablet Hardness Tester

Tablet makers no longer need to rely on the sensitiveness of their fingers to determine the hardness of tablets. F. J. Stokes Machine Co., Philadelphia, Pa. is now offering an instrument which measures tablet hardness directly, expressing this in terms of the kilograms of pressure required to crush the tablet. This reading may then be correlated with the desired

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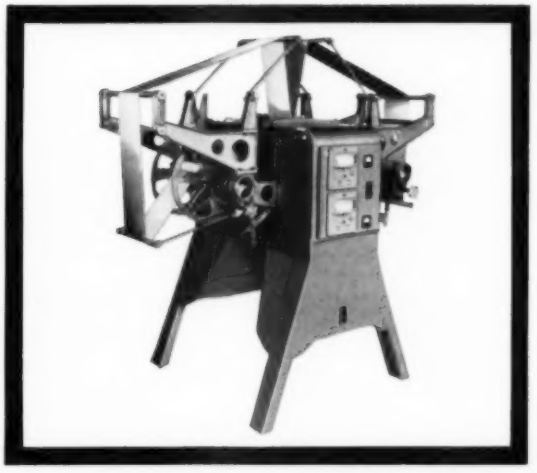

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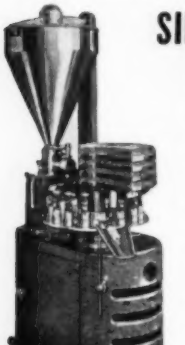

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★ Handles all metal tubes. Model RV-7 from ⅜" to 1½" diam. x 7½" high. RV-10 from 1" to 2½" diam. x 12" high.
★ Two-fold—Three-fold or Quadruple fold on RV-7. Two-fold or Three-fold on RV-10.
★ No tube—no fill. Coding jaws—Automatic Ejector.
★ Cap Tightener.
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physical characteristics of the tablet, its composition and method of manufacture.

With the new Stokes Tablet Hardness Tester, you simply place the tablet on its edge between an anvil and a movable spindle with variable spring-loading, and turn the bolt until the tablet breaks. The difference between the zero and the final readings is the pressure in kilograms required to fracture the tablet. Readings may be estimated readily to an accuracy of 0.25 kilograms.

The Stokes Tablet Hardness Tester is designed to test tablets ranging in size from the smallest practical up to ½ inch in diameter.

A leaflet telling how to use the new Stokes Tablet Hardness Tester contains a tabulation of comparative

data for typical tablets made on single punch and rotary tablet machines. By means of this table, the observed hardness reading (in kilograms) for any tablet can be correlated with its weight, thickness, and density factor.

Copies of the leaflet are available free on request from F. J. Stokes Machine Co., 5500 Tabor Road, Philadelphia 20, Pa.

Floating Blade Evaporator

A new continuous turbulent floating blade evaporator, permitting the thinnest possible films on the heat transfer cylinder and smaller amounts of material in process was introduced by the Rodney Hunt Machine Co., Orange, Mass., at the 25th Exposition of Chemical Industries, Convention Hall, Philadelphia, Pa. Called the Turba-Film Floating Blade Evaporator, the new unit is ideal for reduction of solutions from which the intermediate product is to be a mixture of crystals and liquor. In some instances, it is possible to produce dry powder.

The floating blade evaporator is similar in principle to the company's widely used Turba-Film Evaporator,

differing in one significant respect; the blades of the rotor are pivoted so that they ride on a thin film of liquid flowing down the heat transfer cylinder.

Because of the wiping action of the rotary floating blade system, the action of the heating medium on the thinly distributed product is reduced to a matter of seconds for each particle of the material in process. This is but a small fraction of the time required by conventional circulatory evaporators.

Blades are constructed of metal, nylon, Teflon or other material appropriate to the substance in process. The evaporator is adapted especially for the separation by distillation of heat sensitive materials which, under conventional distillation or condensation, tend to decompose or polymerize, or lose other essential qualities.

The process of distilling or evaporating fluids in the Evaporator is effected with the help of an integral metering pump and foam separator. The apparatus distills any kind of fluid including those which foam badly. Foaming, which often represents waste of end-product in the processing of liquids under vacuum, is controlled in such a way as to entail no loss. Continuous movement of the fluid, impelled by the rotating blades, prevents the formation of crust or coke on the walls of the heating chamber.

The vertical evaporating chamber is jacketed so that it is possible to heat or cool the materials in process depending on their individual characteristics. The interior of the system contains a wiper system driven by V-belt drive from an electric motor. The bearing is externally supported and the drive is through a mechanical seal of appropriate construction. The vanes or wipers spread centrifugally from the shaft by a crank movement to meet the walls of the evaporator.

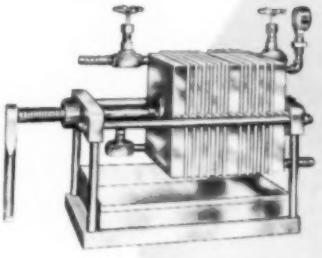
The rotating foam separator prevents the entrainment of droplets which tend to pass off in the vapor stream. These fine drops are thrown by centrifugal force to the outside of the chamber and return to the evaporating section. Each successive element of the floating blade system redistributes the thin-film layer of the material in process.

The evaporator will operate at full efficiency at any available steam pressure. For very high temperatures good results have been obtained by the use of Diphenyl vapor. For products which must be processed at very low temperatures provision is made for warm-water heating furnished by centrifugal pump.

The Floating Blade Evaporator is available in seven sizes with cylinder diameters of 4" to 36" and heating areas of one to 200 sq. ft.

Rodney Hunt also exhibited at the show, their standard Turba-Film Evaporator capable of evaporating up to 5000 lbs. of water per hour. Also included in the booth were photos and information describing the Rodney Hunt-Luwa Spray Dryer. This equipment converts pumpable fluids to dry powders of the desired particle size or to dust-free hollow beads.

The MODERN FILTER



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Advancing Therapy

Drug for Hypertension

A new hypotensive drug, Ecolid 4,5,6,7 - tetrachloro - 2 - (2 - dimethylamino - ethyl)—isoindoline dimethochloride, has been used in the treatment of severe hypertension by R. D. H. Maxwell and T. J. G. Howie (*Bril. Med. J.* 1189, Nov. 12, 1955). Consistent activity by mouth has been confirmed. The initial dose should not exceed 25 mg., and treatment consists of 25 to 200 mg. administered before breakfast, with a dose also during the evening, if required. It is more active than pentolinium, but side-effects are more severe; the duration of action is longer. The combination of oral dosage of ecolid and reserpine has been found useful in the treatment of hypertension.

Malignant Lymphoma

Sixty-two patients suffering from malignant lymphoma have been treated by D. A. G. Galton et al. (*Bril. Med. J.* 1172, Nov. 12, 1955) with *p*-(di-2-chloroethylamino) - phenylbutyric acid (CB 1348), a water-soluble aromatic nitrogen mustard. There were 23 patients with Hodgkin's disease, 11 with reticulum-cell sarcoma, 12 with lymphocytic lumphoma, eight with chronic hymphocytic leukemia, six with follicular lymphoma, one with mycosis fungoides, and one with exfoliative erythrodermia.

Striking remissions were obtained in four cases of Hodgkin's disease, seven of lymphocytic lymphoma, four of chronic lymphocytic leukemia, and five of follicular lymphoma.

CB1348 therapy is relatively free from gastrointestinal side-effects and has proved to be less damaging to hemopoietic tissue than cytotoxic agents hitherto available for the treatment of malignant lymphoma.

Albomycin Antibiotic

Results of laboratory and clinical investigations of albomycin, a new antibiotic prepared in the U.S.S.R. from *Actinomyces subtropicus*, are presented by G. F. Gause (*Bril. Med. J.* 1177, Nov. 12, 1955).

Albomycin is effective against a variety of organisms, and particularly against staphylococci resistant to other antibiotics. Its action is about ten times as strong as that of penicillin.

It forms a reversible complex with the serum proteins, which facilitates its circulation in the body. It is non-toxic, and well tolerated in large doses—up to 50 million units per kg.—given subcutaneously or intravenously. No side-reactions were noted after intrathecal injections in children.

Albomycin has proved effective in the treatment of pneumonia, especially in young children, in the septic complications of dysentery and measles, and in meningitis due to penicillin-resistant pneumococci. It has also been used in the treatment of peritonitis and other surgical infections, and for penicillin-resistant prostatitis and gonococcal urethritis.

Pinworm Treatment

Among a number of related thionocarbanilates studied for anti-pinworm activity in mice by G. W. Rawson et al. (*Antibiotics and Chemother.* 5:642, 1955), *n* - butyl - *p* - allyloxy - thionocarbanilate (Su 2434, Ciba) demonstrated particularly good activity against these parasites. This substance possesses a low degree of peroral toxicity and a relatively wide margin of therapeutic safety.

Mycolutein Antibiotic

From the mycelium of a streptomycete exhibiting unusually broad inhibitory potency a yellow crystalline compound was isolated by H. Schmitz and R. Woodside of J. T. Baker Chemical Co., Phillipburg, N. J., (*Antibiotics and Chemother.* 5:652, 1955). This previously undescribed compound has been named mycolutein.

Mycolutein inhibits a variety of fungi at concentrations of the order of 1 mcg./ml. but shows no activity against a variety of bacteria.

The constant melting point of the compound and countercurrent distribution experiments furnish some evidence of its essential purity. A methanolic solution of mycolutein shows absorption maxima at 254 and 345 mμ, and chemical tests indicate an aromatic nucleus and unsaturation.

Vitamin B-6

It is safe to say according to R. W. Vilter (*J.A.M.A.* 159:1210, 1955) that vitamin B_6 is a very important nutrient that is essential for human beings; however, deficiency states occur only under unusual circumstances, with manifestations in the skin, mucous membranes, and the central and peripheral nervous systems. Most of the therapeutic claims for vitamin B_6 are still beclouded by uncertainties. Though much more investigation will be necessary before the role of vitamin B_6 as a therapeutic tool will be firmly established, clinicians should be alert to the symptomatology of vitamin B_6 deficiency so that they may recognize deficiency states that may be conditioned by new drugs, new food processing methods, and other changes in our daily life that cannot be predicted at this time.

Appetite Depressant

A new appetite depressant, tradenamed Preludin, was announced in the British publication, "Chemist and Druggist" for November 5, 1955. The compound is 2-phenyl-3-methyl-tetrahydro-1,4-oxazine hydrochloride and claims are made that it acts quickly and effectively in curbing the patient's appetite and breaking the psychogenic overeating habit, yet does not affect blood pressure or heart action so that it may be given to patients with cardiovascular disorders and hypertension. Additionally, it is said not to create excessive mental stimulation. The product is to be manufactured and distributed in England by Pfizer, Ltd. for C. H. Boehringer Sohn of Ingelheim am Rhein.

Parenteral Nutrition

Amino acids administered parenterally are utilized for synthesis of the body's protein and can be given to maintain or improve the protein nutrition. Parenteral nutrition includes amino acids and salts and carbohydrates in the form of glucose or fructose together with

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vitamins. By infusion of amino acids with carbohydrates, positive nitrogen or protein balance can be achieved in a number of cases even though the body's caloric need is not covered. If parenteral nutrition is to be complete, amino acids, glucose, and fat must be present in the solution. Fat in an emulsion for intravenous use must be finely dispersed; the aim is usually to keep the diameter of the particles at 0.2—1 μ, according to A. Wretlind, (*Nord. Med.* 53:1013, 1955). Parenteral administration of fat, so that the entire caloric requirement can be met parenterally, is being studied intensively, and routine administration of amino acid-glucose-fat emulsions containing the necessary salts and minerals in conditions where complete parenteral nutrition is necessary is being done on an experimental basis. No method is at present available for producing these emulsions in such a way that they may be administered with adequate freedom from side reactions.

Dysmenorrhea Treatment

This report by W. G. Caldwell (*Rocky Mountain Med. J.* 52:701, 1955) is concerned with the medical management of dysmenorrhea with Fiorinal, a new analgesic and sedative, which contains Sandoptal (isobutylallylbarbituric acid), caffeine, acetylsalicylic acid, and acetophenetidin. The author used this drug in 47 women, whose ages ranged from 18 to 42 years. Thirty-five of the 47 patients had received previous therapy, none with any success. An initial dose of two tablets of Fiorinal, taken at the first sign of cramps, and followed routinely in three hours by one tablet, proved effective in 22 patients. Twenty-five patients required an increased or additional dosage of Fiorinal. Thirty-five of 47 showed excellent response, 18 improving to the point where they no longer required regular monthly medication. No side-effects were noted in any of the 47 cases.

Stable Oral Penicillin

Bristol Laboratories Inc. has been issued a United States patent on the first orally administered penicillin product in a stable, ready-made aqueous form that produces high initial blood levels.

The patent (U.S. Patent 2723938), issued November 15, 1955 to Frank H. Buckwalter and Murray A. Kaplan of the Bristol Laboratories Research Division, covers the use of sodium phytate as a suspending agent for aqueous procaine penicillin formulations as well as the use of sodium phytate to stabilize aqueous suspensions of 1-ephenamine penicillin sufficiently to make possible a ready-made product instead of a dry-mix.

Tests with the drug have shown that one teaspoonful, containing 300,000 units of procaine penicillin, produces blood levels at the end of one, three, six, and eight hours, which are comparable to those yielded by an equal dose of potassium penicillin G. Soluble penicillin salts such as sodium or potassium penicillin G require compounding shortly before use and have only limited stability after preparation.

Antimalarials for Arthritis

The antimalarial drugs Atabrine and Aralen have proved to be of outstanding benefit in a number of severe cases of rheumatoid arthritis, according to L. J. A. Parr (*Medical Journal of Australia*, 2:358, 1955).

The idea of using the two drugs was suggested by their known efficacy in lupus erythematosus.

Evaluating the drugs currently used to treat the disease, Atabrine and Aralen were found to have controlled the condition for years in some cases, when all other remedies had failed. A recurrence is possible four or five months following withdrawal of either antimalarial drug. In some patients, dermatologic reactions occur but disappear after cessation of treatment, after which either drug can be re-instituted.

New Adreno-Hormones

Two new adreno-cortical hormones have been synthesized by a group of investigators at The Upjohn Company headed by Dr. J. A. Hogg. These are 2-methylhydrocortisone and 2-methyl-9 alpha-fluorohydrocortisone and their synthesis was reported in the Journal of the American Chemical Society for December 5, 1955. The first compound is ten times as active as hydrocortisone in the glycogen deposition assay and 2.6 times as active as DOCA with respect to salt retention, so that it may be clinically useful in the treatment of rheumatoid arthritis. The fluorocompound is more closely related to aldosterone in its physiological activity and should be useful in treating Addison's disease. It is 38 times as active as hydrocortisone in the glycogen deposition assay and 90 times as active as DOCA in promoting salt retention. These compounds certainly bear watching and it will be interesting to see what clinical investigations reveal as to their future usefulness.

New Pharmaceuticals

Trinalis Supprettes (William A. Webster Company, Memphis) each contain 2 mg. of 9-aminoacridine hydrochloride, 3 mg. of phenylmercuric acetate, 1 mg. of tyrothricin, 20 mg. of urea, 100 mg. of lactose and 5 mg. of sodium lauryl sulfate in an odorless, greaseless, nonstaining and non-irritating base requiring no refrigeration. The suppositories are intended for the treatment of Trichomonas vaginalis and are also useful in Monilial and non-specific vaginitis. The suppositories are available in jars containing 14.

Topicort Spray (Roussel Corp., New York City) provides 15 cc. of pressurized hydrocortisone aerosol, 0.5 per cent, in a safety-coated glass spray bottle for topical dermatological therapy.

Lorinal (Arnar-Stone Laboratories, Inc., Mount Prospect, Ill.) is chloral hydrate, available in 1.0 Gm. capsules, in 0.5 Gm. capsules and as drops containing 3¾ grains per 0.3 cc. The 1.0 Gm. capsules are available in bottles containing 50, the 0.5 Gm. capsules are packed 100 to a bottle and the dropper bottle contains 15 cc.

Sandril (Eli Lilly and Company, Indianapolis, Ind.), reserpine, is now available in two new forms—a 5 mg. tablet, buff (cross-scored) in bottles of 30 and 500 and as an injectable solution containing 2.5 mg. per cc. in a 10 cc. rubber-stoppered ampoule. Tablets containing 0.1, 0.25 and 1 mg. have previously been available.

Cytoferin (Ayerst Laboratories, Inc. New York) is available in bottles containing 100 and 1000 tablets. Each tablet contains 200 mg. of ferrous sulfate exsic. and 150 mg. of ascorbic acid and the preparation is intended for the treatment of hypochromic microcytic anemia.

Bicillin-Vee tablets (Wyeth Laboratories, Philadelphia) combine approximately 100 mg. (100,000 units) of benzathine penicillin G and 62.5 mg. (100,000 units) of penicillin V to provide both prolonged and high penicillin blood levels on oral administration. The tablets are available in bottles of 36.

Perazil (Burroughs Wellcome & Co., Inc., Tuckahoe, N. Y.) is now available as 25 mg. sugar-coated tablets, packed in bottles of 100 and 1000. It is a long-acting antihistamine, a brand of chlorcyclizine hydrochloride.

PATENT THOUGHTS AND TRENDS

(*Continued from page 69*)

frequently in the past. Instead, organizations such as the A. C. S. should have come of their high ranking *technical* personnel make the actual contacts, concerning themselves with the *technical* phases involved in patent practice and leaving the purely legal matters to the patent bar. Perhaps a cooperative or joint action would be the practical and feasible answer to the matter, it being understood that the function of the technical representatives would not be merely to parrot the patent practitioner but to bring home to the Patent Office the position of inventors on the practical aspects of the problem.

It will be interesting to watch whether the American Chemical Society or other similar organizations will do anything about the Cheesman proposal. If this proves to be just one more proposal about which nothing is done, technical people will only have themselves to blame if the patent bar cannot by itself convince the Patent Office that certain practices are not in the public interest.

The same comments made four years ago appear to apply with equal force today.

It is true that from time to time sincere efforts are made to reach understanding. To the knowledge of the writer, the most recent one occurred a few months ago when, at a meeting of a group of directors of research in New York City, the very topic here outlined was considered during the discussion. Interest was then generated to the extent of arranging for a meeting with the Commissioner of Patents. It is hoped that that interest has been maintained and others interested in this general problem will help actively and continuously.

Recent Patents

2,720,483—Olin Mathieson—Obtaining a Conjugated Estrogen Preparation.

2,720,484—Allied Labs.—Separation of Viral Substances from Animal Tissues.

2,720,485—Allied Labs.—Prepn. of Concentrated, Purified Ultraviolet Inactivated Hog Cholera Vaccine.

MODE OF ACTION OF ULTRA-LOW PRESSURE AEROSOLS

(*Continued from page 47*)

The conventional Two Phase System, including both high and low pressure aerosols operating at about 35 and 70 p.s.i.g. respectively, utilizes propellant as the major constituent in which is dissolved a relatively small proportion of active ingredient.

As the product is dispensed from the container the predominantly propellent droplet immediately vaporizes, leaving fine particles of active ingredient suspended in the atmosphere. The vaporization occurs with such rapidity that the droplet literally explodes into minute fragments, and because of the fineness of the resulting particles, they remain suspended in the atmosphere for relatively long periods of time. This action is graphically depicted in Fig. 4. When a relatively coarse spray is desired, e.g. for surface application, the quantity of propellant is redued, or alternately, a propellant of lower vapor pressure is used.

(to be Concluded)

THE IMPORTANCE OF TODAY'S PACKAGE

(*Continued from page 51*)

incidentally, has been one of the pioneers in the use of multi-color printing on packaging.

Now, the question I am sure you are asking yourselves is: How much did this packaging improvement cost? Actually, relatively little. The biggest single item is the cost of the boxboard. In going from two colors to four, this cost did not change. Also, there was no change in the costs for cutting and creasing, gluing, packing and other finishing operations. Due to improved techniques, the printing itself still remained as one operation. It was merely shifted from a two-color press to four-color equipment. Therefore, the only extra cost was in the preparation of two additional press plates and two additional inks. These are insignificant items in a volume of any size. What was significant, was the tremendous increase in sales that resulted from the packaging change.

The influence of improving techniques of packaging designs is not confined by any means to the food industry. Its influence is being demonstrated in many other consumer fields. By way of illustration, here is a typical example from the tobacco industry.

In designing its new package, Philip Morris was keenly interested in having gold on the package. Both the designer, Egmont Arens, and the company were concerned over whether the printing industry was capable of reproducing a satisfactory gold. As a matter of fact, initial consideration was given to the usage of gold bronze. However, the bronzing operation is too slow for the anticipated volume.

Our company was able to demonstrate to Philip Morris some of the new developments which we had obtained on other labels. We showed that we were able to print a metallic gold by the Gravure process. This was not only the answer for Philip Morris from a quality standpoint, but it also cost substantially less than it would have if bronze had been used.

Let me interject this further thought in answer to this question. We believe it is important on any packaging development to work closely with the purchasing agent and through him with sales, advertising and other people concerned with the development. When any manufacturer is giving consideration to a packaging development the sooner he can take his supplier into his confidence the better. Speaking from personal

(*Continued on page 106*)

Compounder's Corner

Sugar Detergents

At the meeting of the New York Section of the Society of Cosmetic Chemists held November 30, 1955, L. Osipow of Foster Dee Snell presented a paper on "Sugar Esters in Cosmetics." These compounds seem to offer considerable promise as potentially non-toxic detergents, emulsifying and wetting agents with low foam characteristics.

The fatty acid monoesters, which at present seem most interesting, are made by heating together in the presence of an alkaline catalyst a mixture of sucrose and the fatty acid methyl ester. The diester is first formed and prolonged heating converts it to the monoderivative. The stearate was presented as an example, but a variety of other fatty acids have been used. The stearate is a solid which has been formulated to make a number of satisfactory cosmetic lotions and creams; the foaming of solutions is less as the molecular weight of the fatty acid increases. Although tests have not yet been completed, the sugar surfactants are tasteless, are low in irritation and seem to be non-toxic in food and pharmaceutical applications. They leave a soft, velvety feel on the skin and do not produce tacky and sticky cosmetics.

Emulsion Stability

R. Marchisotto, J. E. Christian and G. J. Sperandio (*J. Am. Pharm. Assoc. Pract. Ed.* 16:613, 1955) studied the effect of hard water on the stability of an emulsion. Using an emulsion made under standard conditions from 20 per cent of mineral oil, 10 per cent of glycerin, 6.72 per cent of oleic acid and 3.28 per cent of triethanolamine, the investigators used size frequency analysis to estimate the stability of emulsions made with distilled water, hard water and hard water modified by the presence of disodium ethylene diamine tetraacetic acid. As was expected, but had not previously been published, the emulsions made with hard water were less stable than those made with distilled water or including the sequestering agent.

Comment: The weaknesses in this study are the specificity of the conditions and method of investigation. First, size frequency analysis is in some cases a good method of determining potential instability of an emulsion, but must usually be checked against centrifugation or more particularly against actual shelf life. Furthermore, it is chemically obvious that an emulsion can be stable only as long as its emulsifying system remains intact: the addition of calcium and magnesium salts to an emulsion system based upon a water-soluble soap will inevitably have some effect upon the stability of the system. I would guess, indeed, that the effect of these additions would differ with the soap used. Finally, and the authors are of course aware of this, hard water may have little or no effect upon systems using non-ionic emulsifiers or ionic emulsifiers that are not soaps. I believe that the application of this study should be limited to the effect of hard water upon the size frequency distribution in a triethanolamine oleate—mineral oil emulsion.

Coal Tar Ointment

A one per cent crude coal tar ointment, in which the tar is finely divided and dispersed uniformly by the addition of 0.5 per cent of polyoxyethylene sorbitan monolaurate (Tween 20), a nonionic surfactant, prior to incorporation with zinc oxide paste, has proved to be clinically effective according to R. G. Carney and L. C. Zopf (*A.M.A. Arch. Dermatol.* 72:266, 1955), while producing about one-fourth as many reactions of cutaneous irritation as occurred in the use of two per cent and five per cent crude coal tar in zinc oxide paste prepared by standard methods.

Ointment Base

Plastibase and Plastibase Hydrophilic are new bases used in a number of ointment products manufactured by E. R. Squibb & Sons, and available to pharmacists for compounding prescriptions. Plastibase is non-water-absorbing and contains 95% liquid petrolatum, U.S.P., and 5% polyethylene. Plastibase Hydrophilic, which can absorb ten times its weight of water, is made up of 88.16% liquid petrolatum, U.S.P., 5.64% polyethylene, 6% emulsifying agent, 0.1% antioxidant, and 0.1% preservatives to prevent mold growth after the addition of water.

Although the drugs contained in ointments are chosen for specific healing actions, the ointment base may significantly limit the drugs' efficacy. Factors such as the amount of the drug released by the ointment within a specific period of time, the length of time the drug continues to be released, the dispersion of the drug within the ointment itself so that there are no irritating concentrations, and the effects of temperature changes on drug release, must be taken into consideration for maximum healing efficacy. Controlled laboratory tests carried out at the Squibb Institute for Medical Research have shown Plastibase superior in each of these respects to many popular ointment bases now in use.

Amberlite Resins

Rohm & Haas Company, Philadelphia, is offering a set of new analytical grade resins:

Amberlite IRA-400 (Cl) Analytical Grade is a strong base anion exchanger which derives its exchange activity from quaternary ammonium groups. It was previously available in the hydroxyl form. Now it is being supplied as the chloride form rather than the hydroxyl form because the chloride salt of strongly basic exchangers does not require great care in handling to prevent adsorption of acidic materials, particularly carbon dioxide, normally present in the atmosphere.

Amberlite IRA-401 (Cl) Analytical Grade is a strong base anion exchanger of high porosity. It is a porous analog of Amberlite IRA-400. Amberlite IRA-401 is supplied in the chloride form for the same reason as that given above for Amberlite IRA-400 (Cl). As a result of the high porosity of this exchanger, it is of particular interest in the adsorption and fractionation of high molecular weight materials.

Amberlite IR-45 (OH) Analytical Grade is a weakly acidic anion exchange resin which derives its activities from primary, secondary, and tertiary amine groups. It replaces Amberlite IR-4B. Amberlite IR-45 can be operated at temperatures as high as 2/2° F., and is

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superior to IR-4B with respect to physical and chemical stability.

Technical notes describing the Analytical Grades of these exchangers are available on request. The bulletins on Amberlite IRA-401 (Cl) and Amberlite IRA-400 (Cl) contain simple procedures for converting these resins to the hydroxyl form.

Calcium Thioglycollate

Calcium thioglycollate, or calcium mercapto-acetate, has the following properties. It occurs in fine, colorless needles, crystallized with three molecules of water. Its molecular weight is 184.2. Aqueous solutions of 2.5 per cent of this material have a pH approaching 11.5. Traces of iron turn it red.

The use of the calcium salt of thioglycollic acid has been recommended for use in the tanning industry as a depilatory for crude skins. This does not cause swelling of the proteins, and at the same time softens the skins.

Calcium thioglycollate is used in the cosmetic industry in the form of depilatory creams and lotions. It is non-irritant and, unlike the sulfides, does not possess an unpleasant odor. The pH of the preparations is usually higher than 10, the practical concentrations varying between 2 and 5 per cent.

Micro-Cel

A new line of synthetic calcium silicates, called "Micro-Cel," has been announced by the Celite Division of Johns-Manville.

Produced by the chemical combination of lime and diatomaceous silica, Micro-Cel is a powder available in specific grades which offer a wide range of physical properties. The powder will absorb 1 to 2½ times its weight of liquids and still remain a free-flowing powder. Different Micro-Cel grades with particle sizes as low as 0.02 microns and particles of rounded to spherical shapes, provide fast, uniform blending without segregation. Various degrees of viscosity up to a paste or semi-solid can be achieved by adding relatively small quantities of Micro-Cel, while its high absorption and fine particle size of less than 0.1 micron effectively controls caking of deliquescent products and insures flowability even after prolonged storage. A small percentage of this calcium silicate materially increases the bulk of dry powders and allows control of package density and its surface characteristics, fine particle size and large specific surface combined with inertness indicates its value as a pigment extender. Micro-Cel's different combination of properties provide aid in suspension of heavier solids, its high absorption, fineness and particle shape indicate its value as a flatting agent, and the combination of fine particle size, particle shape and wetting characteristics suggests the value of Micro-Cel as a reinforcing pigment.

This combination of properties makes Micro-Cel obviously attractive for investigation in face powder formulation, and it may well prove to be valuable in other types of products. The composition of the product is such as to suggest absence of toxicity in cosmetic applications, but this should be verified.

Magnesium Trisilicate

Magnesium trisilicates which conform to the present B.P. requirements can vary markedly in their physical characteristics as well as in their efficiency as antacids, according to J. A. Armstrong et al. of Boots Pure Drug Co., Ltd. (*J. Pharm. Pharm.* 7:862, 1955).

Investigation has shown that the less crystalline the sample of magnesium trisilicate the higher the antacid efficiency when measured *in vitro*.

It would appear that antacid activity of magnesium trisilicate is associated with the degree of distortion of the crystal structure, and that this distortion is possibly related to the amount of "combined water" in the crystal and the way in which this is included in the lattice. A magnesium trisilicate with a high degree of distortion of its crystalline structure gives a better antacid control *in vitro* than does one which is more crystalline.

Procaine Penicillin Tablet Stability

An experiment by R. Levin (*J. Pharm. Pharm.* 7:870, 1955) shows that when stored at temperature of 4° C., 18° ±5° C. and 37° C., procaine penicillin tablets showed a potency loss not greater than four per cent after nine months. This loss is not increased by storing the tablets in a large insecurely sealed bulk container. The evidence appears to suggest that potency losses brought about by the presence of free moisture are due rather to residual moisture in the original tablets than to that taken up during subsequent storage. If this be so, a lower initial free moisture content might be expected to reduce or eliminate the small potency loss sustained by the test samples. A slight increase in the time for disintegration was noted with aging, this being greater as the temperature of storage increases. Tablets stored for nine months at 37° C. disintegrated completely within two minutes. The free moisture content showed very small increases, the greatest taking place at the lowest storage temperature. Procaine penicillin tablets have been stored in sealed jars, in a large loosely capped jar and in an open jar, in an effort to detect a tendency to deterioration either by potency loss or in other respects. Within the limitations of the test, namely time and condition of storage, it would appear that tablets of procaine penicillin are relatively stable in atmospheric conditions normal to England, even where they are not packed in a tightly sealed container.

Optical Bleaches

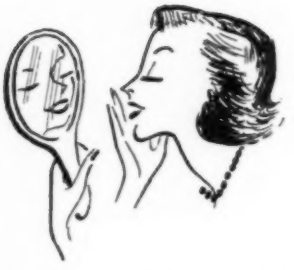
Compounds which show a blue or blue-violet fluorescence in daylight are useful in certain products as whitening and brightening agents. Until recently they have been employed mainly as whiteners for textiles and paper but they are now finding applications in other fields. White cotton cloth which has become yellowed shows maximum absorption of light in the vicinity of 4700 A in the blue band of the visible spectrum. The compounds used as "optical bleaches" absorb ultra-violet light and emit a pure blue light of a wave-length close to 4700 A. Adding this blue light to the yellowish light reflected from the cloth produces white light.

To be useful as a whitening agent, a fluorescent compound must be water-soluble and practically colorless, i.e., it must not absorb much light in the visible range.

It is reasonable to expect that some of the fluorescent brighteners eventually will be used in shampoos and hair rinses. Stearns mentions that optical bleaches incorporated in shampoos are very effective for brightening grey hair. When applied to blond hair they give the brightness of a halo. The fluorescent brighteners are useless on brown or black hair.

The question of toxicity must be considered in selecting fluorescent brighteners for use in cosmetic products. None of the optical bleaches are included in the list of dyes certifiable by the Food and Drug Administration at the present time, although this does not mean that they are toxic. The coumarin derivatives which have been used in soaps for some time presumably are safe for use in shampoos. However, any stilbene derivatives should be investigated carefully for toxic or irritant properties.—*Schimmel Briefs.*

Skin Research



Percutaneous Absorption

Strictly speaking, the term percutaneous administration should be confined to the use of preparations on the intact skin surface with the intention of obtaining sufficient absorption of the medicament to produce a systemic effect. The term has, however, become more widely applied to include the use of external preparations for the purposes of obtaining a localized action of the drugs deep in the layers of the skin or in the underlying subcutaneous tissues.

This method of administration while offering certain advantages is unlikely to have more than a very limited application in clinical treatment. It has the advantage that substances which are inactivated in the alimentary tract or cause gastric irritation can be given by this route without the necessity of an injection. However, the effective control of dosage presents serious practical difficulties. Percutaneous administration is mostly used when a localized action of the drug is required in a particular region of the body and, occasionally, for the administration of drugs which require their concentration to be built up gradually and then maintained at a constant level by daily inunction. It is commonly employed to obtain the local effects of the sex hormones, and, in the past, it has been used for the administration of mercury.

In the last few years, the inclusion of estrogens in cosmetic creams has increased the interest in the percutaneous absorption of these substances. Although the reports indicate that there may be little danger from the intermittent use of estrogen cosmetic creams in the amounts recommended, the possible dangers of indiscriminate use should not be overlooked. Progesterone is also absorbed on percutaneous administration but not so easily as the estrogenic hormones. This is surprising in view of the close similarity in chemical structure and high solubility in organic solvents of these substances. The percutaneous administration of progesterone has not been used clinically.

The percutaneous absorption of the male hormone, both as free testosterone and as its propionate, has been effectively demonstrated in experimental animals and applied in clinical medicine. It has been shown that free testosterone is more effective on percutaneous administration than the propionate and that it is more effectively absorbed from a solution in alcohol than from a solution in oil or ointment. Testosterone propionate has been administered percutaneously in the treatment of dysmenorrhea and for this condition a solution in sesame oil is more effective than an ointment. In other clinical conditions, both in the male and female, percutaneous administration has proved of value in obtaining a local effect by applying minimal doses to a given area of the skin and thus avoiding undesirable systemic reactions.

Since their introduction, cortisone and more recently, hydrocortisone, have been extensively used for the topical treatment of a variety of dermatological conditions. The basic steroid structure of these compounds suggest that they may be as readily absorbed percutaneously as the sex hormones. However, it has been shown that local application of hydrocortisone, in a total dose of 750 mgm., applied to the skin over a three-day period in a washable ointment base, failed to produce an increase in the 17:21-dihydroxy-20-ketosteroids in the urine and blood.

As would be expected, the fat-soluble vitamins are more readily absorbed through the skin than are the water-soluble vitamins. Vitamin A is absorbed through the skin of vitamin-A deficient animals in amounts sufficient to restore growth and cure xerophthalmia.—J. W. Hardgraft (*Pharm. J.* 316, 1955)

Mucunain and Itching

Cowhage is the name given to the short barbed spicules covering the seed pods of the tropical plant Mucuna pruriens. These spicules have long been respected both as a vermifuge and as an effective stimulus for itching.

It has been found possible to produce itching in man in the absence of all clinical signs by the intraepidermal insertion of a single cowhage spicule.

The active pruritogenic principle of cowhage has been isolated, purified, and identified by W. B. Shelley and R. P. Arthur of the University of Pennsylvania School of Medicine (*A. M. A. Arch. Dermatol.* 72:399, 1955) as a new plant proteolytic enzyme: mucunain.

It is postulated that the activation or release of tissue or serum proteinases in the epidermis may be the basis for clinical pruritus, since proteinases are uniquely pruritogenic.

Finally, attention is directed to the fact that mucunain probably is responsible for the activity of cowhage against intestinal worms.

Hormones and Apocrine Glands

It has become apparent that the axillary apocrine sweat gland in man is under endocrine control, since its very development and function heralds puberty. Furthermore the hormonal changes associated with pregnancy or the menopause may produce striking functional and histologic changes. Studies by W. B. Shelley and M. C. Cahn of the University of Pennsylvania School of Medicine (*J. Invest. Dermatol.* 25:127, 1955) consisted of a histologic investigation of the effect of a wide variety of hormones on normal *human* axillary skin. Only clinically feasible dosages were employed and the period of topical as well as systemic treatment was kept constant at three weeks.

Careful study both clinically and histologically did not reveal any significant changes between the treated and untreated axillary skin. The apocrine sweat glands, in common with the hair, sebaceous glands, eccrine glands, epidermis, and corium, appeared unaffected by either the three week course of topical or systemic hormonal therapy.

One striking clinical change did however occur. All the subjects receiving *progesterone* systemically, either alone or in association with ethinyl estradiol or testosterone, noted generalized hy-

peridrosis. This appeared after several days of treatment and persisted until treatment was stopped. This finding sheds light on the etiology of the hyperidrosis which commonly occurs in pregnancy and at the menopause. It would seem that high levels of progesterone have a central stimulant effect on the regulatory neural control centers for the eccrine sweat gland. This observation deserves further study.

Comment: Testosterone and progesterone were tested topically as wet packs applied for 30 minutes daily for three weeks as solutions in 95 per alcohol in concentrations varying from 1:10 to 1:100,000. These are not necessarily optimum or even especially good conditions for attaining perculaneous absorption in quantities sufficient to cause substantial local concentrations. This portion of the investigation may warrant restudy.

Epidermal Proteins

The experimental evidence to date indicates that the structural proteins of epidermis are associated with the tonofibrils as the precursors of keratin, according to C. Carruthers et al. (*J. Invest. Dermatol.* 25:89, 1955). The tonofibrils may also play an important role in the adhesiveness of squamous cells. Information concerning the role of the fibrous protein in keratinization has largely accumulated from X-ray diffraction studies on epidermis and hair follicles. Based on differences in the chemical behavior of the pre-keratins of the hair follicle and the results of X-ray diffraction studies, Mercer has formulated an interesting theory of the process of keratinization. In the lower and intermediate layer of the Malpighian stratum the molecules of the primary proteins of unknown shape or size may exist as organized particles of a corpuscular type protein. End to end linkage of the latter in the upper. Malpighian zone brings about the formation of a fibrous form of the protein. Since the protein in fibrous form, in contrast to the hardened keratin, is digested with trypsin and 2 N hydrochloric acid and is converted into the disorganized β form in water at 90 to 95° C. for 30 seconds, Mercer postulates that this fibrous form is held together by hydrogen bonds and salt linkages. The prekeratin zone is dissolved by a saturated urea solution, while in the area of keratinization this solution causes swelling, the degree of which decreases as the hardening becomes more complete. In the zone of keratinization the formation of disulfide linkages between the protein chains occurs since a reversal of the solvent action of urea follows reduction of the —S—S— bonds by zinc and hydrochloric acid. Finally stabilization or formation of true keratin by cystine bridges appears to be brought about by the establishment of covalent links between the protein components in the direction of the fiber. Recent evidence indicates that keratin contains not only —S—S— linkages but also sulfhydryl groups.

Fungal Drug Resistance

The original observations of Murphy and Rothman, Sing and Vilanova and Casonovas that dermatophytes can be made resistant to the fatty acids and that this resistance is of a low order is confirmed by the present studies by E. Grenberg and E. Titsworth of Hoffmann-LaRoche, Inc. (*J. Invest. Dermatol.* 113, 1955). Results of a similar nature were also obtained with 2-Dimethylamino-6- (β-diethylaminoethoxy) benzothiazole dihydrochloride (Asterol). The somewhat greater degree of resistance observed with Asterol may possibly be due to two factors. The first is that this substance offers a much larger range of concentrations within which it may develop resistance. Secondly, the increase of resistance occurs only within that range of concentrations in which atypical growth normally develops. Resistance to a fully fungistatic concentration was not observed.

Acne

There are many pathological conditions that never endanger but often ruin life. Foremost among these according to S. Rothman (*J.A.M.A.* 159:1124, 1955) "harmless" conditions is acne of the adolescent, which in its more serious forms extends well into the third decade of life and in its scarring variety may leave unsightly pockmarks visible through a lifetime.

Progress has been made during the last decade in a better understanding of the local pathogenesis and hormonal constellation of seborrhea and acne. Nutritional and climatic influences have become better appreciated, and the role of bacterial infection has been analyzed; but real progress in therapy is still missing. While the role of "androgenic" hormonal effects on sebaceous glands and cornification of the follicular openings is fairly well understood in both men and women, the main hurdle in the therapeutic use of this knowledge is that the dosage of estrogens required to counteract the acnegenic effects is so high as not to be safe. Whether small and safe doses of estrogens, administered systemically or locally, are effective at all is still a controversial question. Therapy with vitamin A has a good rational foundation because of its well-established antikeratinizing action, but, again, its true therapeutic effectiveness is doubted by many. Modern antibiotics are often valuable in combating the pustular elements of acne, but they do not solve the basic problem.

Thus the main body of our therapeutic armamentarium is still local treatment on an empirical basis as it has been practiced for almost 100 years, and, among topically applied chemicals, sulfur is still the most effective agent. The precipitated sulfur of the United States Pharmacopeia has an optimal particle size that can be incorporated uniformly into any kind of vehicle and is effective without being unduly irritating. Sulfur enters the skin easily and is reduced there to sulfide and hydrosulfide ions. In this form it exerts its keratolytic and sebum-reducing effects. Salicylic acid and resorcinol often added to sulfur preparations for local application act mainly as keratolytics and pacemakers for sulfur. Ultraviolet rays have a similar action, in addition to increasing arterial blood flow.

Estrogenic Hormone Creams

To demonstrate the effects of estrogenic hormone cream on facial skin, H. T. Behrman (*J.A.M.A.* 155: 119, 1954) tested a group of 31 women, all over-thirty-five and up to sixty-five years in age. They were selected on a basis of intelligence and faithfulness to testing procedures, as indicated by their records of performance in similar procedures. The only clinical changes observed from both subjective and objective standpoints consisted of a lessened degree of dryness in facial skin that was previously of a dry type. No appreciable difference was visually observed in the side treated with an estrogenic hormone cream as compared with the side treated with either the identical base without hormones or a commercial night cream having a composition similar to that of the hormone cream. This study demonstrated that noticeable improvement in the appearance of the skin can be obtained through regular use of an emollient cream on women with dry skins. It did not demonstrate that the addition of hormones to such emollient bases increases this improvement to any discernible extent.

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Readers' Questions . . .

Quinine Hair Pomade: *We have noticed on the labels of several hair pomades that they contain quinine. What is the amount of quinine to be used in such pomades and what is the antiseptic value?* NEW ORLEANS.

In formulas for hair preparations that we have seen the amount of quinine contained varies from 0.2 to 0.5 per cent. According to the United States Dispensatory, "While the general antiseptic value of quinine is comparatively low it has marked bacteriostatic properties against certain specific organisms."

Protective Hand Lotion: *Some of the newer hand lotions are featuring skin protection, healing, and bacteriostatic action. Since the ideas certainly have considerable merit and the market should soon become quite large because of the promotion being put into it, I would appreciate suggestions from you for formulating such a preparation.* NEW YORK CITY

The silicones seem to have made a substantai impression on cosmetic formulation, since they have special properties that are quite attractive. They seem to give to the skin, along with expected water repellancy, a smooth feel that is desirable. Allantoin, described at length in an article by S. B. Mecca in the June 1955 issue of this magazine has useful healing characteristics and hexachlorophene has now become virtually standard for its bacteriostatic action. Using these components, the following formula should be a useful starting point for the preparation you wish to make:

Silicone	**2.0**
Allantoin	**0.2**
Hexachlorophene	**0.2**
Glyceryl monostearate	**4.5**
Cationic emulsifier	**0.3**
Glycerin	**5.0**
Water	**87.8**

The glyceryl monostearate is the pure grade, of course, not including the customary potassium stearate as the primary emulsifier, since this would be incompatible with the cationic emulsifier. Citric acid should be added, as required, to bring the pH of the preparation into the 4.5 to 5.5 range for normal skin. As a matter of fact, it might well be advantageous to add enough citric acid and sodium citrate together to form a buffer system that would tend to counteract the alkalizing action of soaps.

Insect Repellant: *Have you any information you can transmit to use on the formulation of modern insect repellants?* MEXICO CITY.

A generally satisfactory insect repellant mixture consists of three parts of dimethyl phthalate, one part of indalone and one part of ethylhexanediol. This mixture can be used as is or as an aqueous alcoholic solution. For an exhaustive study of this subject we recommend that you refer to the article by M. A. Lesser, "Modern Insect Repellants" in the December 1954 issue of this magazine.

General Purpose Lotion: *I am interested in obtaining a formula for a lotion that can be used for after a shave and skin toning purposes, and possibly also as an after-bath rub. Do you have such a formula available?* BROOKLYN.

A lotion of the kind you want is formulated along the following lines:

Boric acid	**2.00**
Menthol	**0.05**
Glycerine	**2.00**
Alcohol	**9.00**
Witch Hazel	**86.95**

Add color and perfume as desired.

Soap Manufacture: *In a course given at a local vocational school we wish to illustrate soap making, but so far have had no success in developing a procedure that will give consistent results in the hands of the students. Any suggestions you may have to offer for a "fool-proof" method of preparing soap will be appreciated.* MILWAUKEE.

I doubt very much that an easy, reproducible method by which students can turn out experimental batches of soap is possible. As you have already discovered, small variations in the composition of the fats will make all the difference with respect to the properties of the finished product. I suggest that you investigate the use of free fatty acids (using mixtures from coconut and palm oils and tallow) along with mixtures of sodium and potassium hydroxides and triethanolamine, depending upon whether you want hard, soft, or liquid soaps.

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(*Continued from page 96*)

experience we have worked secretively on many packaging developments in recent years and we have been able to be of assistance to the manufacturer in the early stages of the development.

One of the major objectives of the carton manufacturer is to keep step with the needs of the product manufacturer, his customer. In the growing trend towards more self-selection shopping and impulse buying, the package looms more and more important as a marketing tool. We believe that the product manufacturer will need to give more and more attention to his packaging to keep it abreast of competition. Indications are that this will mean a wider use of color and more intricate designing. This is a challenge to our industry. I am glad to say that we are prepared to meet it.

What is today's concept in Package design?

FRANK GIANNINOTO, FPDC, PACKAGE DESIGNER

Many firms are facing new packaging problems today, particularly companies which have a whole *line* of products to sell, some of which are self-service. So many companies have products that are coming off the back shelf where they had to be asked for, and are on full view on shelves where customers help themselves.

The supermarket has opened up tremendous new markets for many businesses other than food, as we all know, and with marketing problems constantly changing, packaging concepts have changed, too.

In order to examine some of the new concepts of package design, let's *take* a drug company like Squibb, Lilly or Park Davis and see how the concepts of modern package design actually help *cope* with changing market conditions.

The first job packaging has to do when the product is taken out of a special class, like the prescription or proprietary class, and put into the mass consumer class, is to create an *identity* for the line.

Often study of a line of products reveals strong acceptance for *one* product over the *others*, which are visually unrelated in their packaging and do not share the same brand name. Through package design *ils* prestige can be lent to other items in the line, which *all benefit* from reinforcing the identification.

Creating a distinctive trademark is the first step in establishing this all-important identity, whether for one product or a whole line. A simple, unconfused symbol can create a friendly attitude of acceptance toward *any* product, but is of *special* value in the case of products like drugs, where it has to do a big job of reassurance. A drug product needs a trademark that convinces the consumer that the brand is of unquestionable integrity and quality, that what's inside is *good* for her and even that it's actually pleasant to take.

Through package design a product can seize important marketing advantages in the face of stiffening competition and rising production and marketing

costs. Naturally, any line of products which has to be packaged can benefit from the convenience and economy factors incorporated in a functional package such as dispensing, stacking and shipping.

Mr. Callaghan, do you really think management should be bothered with packaging decisions, which are necessarily technical and are only occasionally concerned with sales?

WRAY CALLAGHAN, EASTERN SALES MANAGER, ROBERT GAIR COMPANY, INC.

I am very firmly of the opinion that packaging decisions today must necessarily be a concern of top management. The packaging industry today is a 12 billion dollar or better industry. It is still very definitely a growing industry.

Packaging can no longer be considered primarily from the standpoint of a container for a product. Packaging today is a major merchandising force and warrants the fullest consideration of top management, together with major decisions on merchandising and advertising programs. More than ever, the folding carton is a real medium for the expansion of sales.

A visit to super markets and comparable merchandising outlets emphasizes more than ever the part that folding cartons play in the day to day decisions of the ultimate consumer. The growth of packaging and the contemplated growth over the coming years of our own industry stresses this point and demonstrates the need for top management supervision of packaging problems, not only for present problems, but in long range plans for the future.

I do not agree that these packaging decisions are necessarily technical and so not concerned with sales. I believe they are directly concerned with sales and can, under proper management guidance become a tremendous force in the ever-growing merchandising system of this country. It is not enough to have a technically good package or a good package from a sales standpoint. They've got to work together under the supervision of top management.

Do you think the interest of top management in packaging is a trend?

EGMONT ARENS, FPDC, INDUSTRIAL DESIGNER

The tremendous potential for sales and good-will of every corporation's "visual assets" is transforming the evaluation of these assets into a top management function.

Modern management, as typified by Philip Morris, is increasingly aware that their companies' visual assets and liabilities do not remain static in the midst of changing markets and consumer demands. "In fact these assets demand of management the same constant attention and evaluation as corporate financial assets."

There is, I detect, a nationwide trend toward continuous top management consideration of its own visual public relations. These include not only prod-

(Continued on page 110)

have you tried

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Modulan is extremely hydrophobic — does not form greasy emulsions and is practically odorless. Because of its outstanding compatibility with oil-in-water emulsions and with soaps and shampoos, Modulan is particularly recommended for use in creams, lotions, baby products, hair preparations, make-up, and ointments.

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Perfumer's Shelf

Perfume Chemicals

In the first experiment, bodies of what might be called the Jasmin group were used.

Pure Amyl Cinnamic Aldehyde, in the pure state was found to have an excellent odor and to be absolutely free from the usual by-odors, and the same can be said of pure Benzyl Acetate and pure Benzyl Alcohol, in which one could not detect any trace of cyanic or benzyl ether by-odors which give high-class compositions a distinctly chemical note. The three above-mentioned were considered excellent products.

A number of Jasmin compounds were made to assess the value of the above: these were selected so that the amount of these bodies would be a large percentage of the formulas. So as not to confuse the issue, trace bodies and natural products were eliminated from the skeleton formula.

In all the formulas made afterwards, greater intensity and delicacy were noticed when using the pure bodies, and the results were much superior than when using the commercial articles. The results make one wonder whether the same results would be obtained when used in soap. If so, the increased cost might be offset by the lesser amount of perfume needed, but up to now, experiments have not been carried out with this end in view.

Jasmin Bouquet

5	Methyl Anthranilate
50	Phenylethyl Alcohol
200	Linalol
350	Pure Benzyl Acetate
100	Linaly Acetate
30	Cinnamic Alcohol
1	para-Cresol
1	Indole
100	Pure Benzyl Alcohol
163	Pure Amyl Cinnamic Aldehyde
1,000	

In the second experiment, another group of bodies, particularly pure Geraniol and pure Citronellol, were tested extensively for their effect on Rose compounds.

Pure Geraniol has been found excellent, lacking the rather objectionable pruny note found in so many commercial products, and after testing samples obtained from various raw materials, it was found that to all intents and purposes they were so near to one another as to make no material difference. When tested against good quality commercial geraniol obtained from palmarosa, the difference was very marked.

The usage of one or other depends on the objective required, as the commercial geraniol ex palmarosa retains traces of bodies which can be very useful in blending, and give a special character and lift which is absent from the pure Geraniol.

A skeleton rose-type compound was made and variations worked out.

Rose Compound

250	Citronellol
300	Phenylethyl alcohol
370	Geraniol ex Palmarosa
10	Geranyl Acetate
40	Linalol
20	Ionone Alpha
10	Nonylic Aldehyde
1,000	

The geraniol from palmarosa gave a softer "departure" and toned down the fatty aldehyde quite appreciably, due to those trace bodies previously mentioned, but on standing on test papers, the pure Geraniol appeared to have more power and, perhaps, a more rosy note than the former material. The same results were obtained in a more complicated formula.

Pure Citronellol and the commercial article were tested in a number of formulas, and in these tests l-Citronellol from Geranium Bourbon was also compared. Pure Citronellol has a very clean smell and lacks totally that by-odor which can be perhaps best described as like that of stale petroleum jelly. Unfortunately, this note appears to be a characteristic of many commercial products. Here, compared with commercial Citronellol, the results were much superior, especially in Tea Rose type odors where pure Citronellol gives a certain brightness to the composition. But in Red Rose blends or imitation Bulgarian Otto, it was found the l-Citronellol from Geranium Bourbon, or better still, the Rhodinol from the same source gave a mellowness and richess which were absent when using commercial Citronellol.

Pure Methyl phenylacetate is another body with a clean odor. As the amount generally used is very small, except perhaps in the case of honey type odors, the higher cost of this pure chemical would not appear to matter a great deal.

Pure Iso-Butyl Phenylacetate. In this case, a very great difference was noted between the pure and the commercial body. In the former, a much more marked flowery character was apparent, and also a delicate apricot note, and a total absence of cyanic odor.

Pure Iso-Amyl Salicylate: Here again the cleaner note and apparently greater power has many advantages, such as when making a Trefle formula. It was noticed that the perfume had a greater buoyancy and that the citrus note of a Bergamot was greatly enhanced, resulting in a more harmonious note.

Pure Linalol and pure Linalyl Acetate were found to be a very great improvement on the best standard qualities and in both cases the cineole note was totally absent. The most remarkable thing was that both appeared to have a much greater power over the standard grades than their apparent contents of Linalol and Linalyl Acetate would indicate. It might be possible that trace bodies in the commercial articles have a neutralizing effect on the main constituents. This was also noted with pure Benzyl Acetate.

An Origan-type of formula was compounded, containing 10 per cent of Carnation compound, 10 per cent Bergamot, five per cent pure Linalol, 10 per cent Heliotropine and 20 per cent Alpha Iso Methyl Ionone as the main ingredients, and the odor of the finished perfume was most gratifying. The Alpha Iso Methyl Ionone has a very smooth and suave odor and no doubt will be found useful to compound modern French bouquets.

Pure Phenylethyl Alcohol and pure Hydroxycitronellal have excellent clean odors and they have been classed together for convenience in making Lily-of-the-Valley type compounds which also provided the opportunity of includ-

ing pure Linalol which had been tested previously.

A typical skeleton formula used for the preliminary test was as follows:

400	pure Hydroxycitronellal
150	pure Phenylethyl Alcohol
100	Cinnamic Alcohol
100	Terpineol
50	pure Linalol
40	Heliotropin
50	pure Amyl Cinnamic Aldehyde
80	Rhodinol
10	pure Benzyl Acetate
20	Ionone Alpha
1,000	

The results of this were found to be an improvement on the use of commercial grades. Finished formulas were compounded containing natural bodies and other odorous chemicals in traces, so as to give a bouquet, and here the real value of the pure chemicals was very apparent.

In conclusion it must be pointed out that, in the main, the pure chemicals are not interchangeable with the commercial bodies, inasmuch as they have a different effect, but their judicious use will, undoubtedly, be a great help in high-class perfumery.—*J. F. Charpy* in *Soap, Perfumery and Cosmetics.*

Flavor and Odor

The many odors that man can distinguish undoubtedly add materially to the enjoyment of foods according to E. C. Clark and H. W. Dodge, Jr. (*J.A.M.A.* 159:1721, 1955). The ability to perceive sweet, salty, sour, and bitter sensations in the mouth is one of the most fundamental building blocks of this sensory composite. The widespread location of the taste buds on the tongue, palate, and nasopharynx gives a man a maximal opportunity to sample each morsel of food before swallowing it. However, the act of perceiving flavors is not a simple mental combination of odor and taste. All of the sensations experienced in the mouth, nasopharynx, and adjacent structures are important. For example, the temperature end-organs in the buccal cavity are our main source of information concerning the hotness or coldness of a substance at the time of eating. Most Western peoples are accustomed to a hot cup of coffee, and this coffee at room temperature is less palatable, both because of its temperature and because of its lack of aroma.

Pain is another important oral sensation associated with flavor. It prevents admission of noxious substances to the alimentary tract and, paradoxically, adds to the enjoyment of food; for example, no connoisseur of Mexican food would be entirely satisfied with a "bland" hot tamale. The wetness or dryness of foods can alter the flavor considerably, both from the standpoint of the sensation produced in the mouth and from that of the chemical changes within the food produced by hydration or dehydration. Likewise, chemical changes produced in the food by saliva may play an important part in certain instances.

The end-organs of light touch and deep pressure are utilized by the mouth, alone, together, or in combination with other sensation. Although difficult to analyze, sensibilities that play important parts in the contribution of oral sensations to flavor are vibration and other sensibilities mediated by way of the teeth and bones of the jaws, impulses from the muscles of mastication and expression, two-point discrimination, and stereognosis. Such terms as texture and consistency represent qualities of foods that elicit composites of many of these oral sensations. A food that exemplifies both of these qualities, as pointed out by Crocker, is taffy. This "chewy" candy is pulled by machines (or by hand) to develop brittleness and fibrous texture, which stimulate more desirable sensations and improve flavor.

One cannot, however, limit flavor to olfaction, taste, and the somesthetic sensations of the oral cavity. Vision, hearing, and the psychological state of the person at the time of eating the food also are important. Vision, for example, plays a prominent part, though one difficult to evaluate, in the perception of flavor. Hearing enters into the perception of flavor in many ways. Modern advertisers recognize this in their use of such terms as crunchy and crackling, words with strong auditory components. The psychological state of the person at the time of eating may affect his perception of flavor. This psychological component has many facets. Among these, at least in part, are those just mentioned: vision and hearing. Also involved are the memories of previous experiences with the flavor, the interest the person has in food, and the setting in which the food is being eaten.

Thus, extraolfactory sensations often play major roles in the perception of flavor. However, as already has been mentioned, this does not necessarily imply that olfaction is not, at times, of primary importance in this regard. Rather, it suggests that olfaction may be one of the basic elements used in the final cerebral synthesis of flavor and that individuals may vary in their dependence on one sensation (smell, temperature, and taste for sweet, salt, or sour flavors, and so on) or another, in accordance with the sensory patterns learned previously.

This concept that flavor is a synthesis of many different sensations, in which olfaction plays a role of varying importance, raises certain semantic questions. As the word "flavor," thought to be derived from the old French term *flaur, fleiur*, meaning smell, is defined in the Oxford Dictionary as "the element in the taste of a substance which depends on the co-operation of the sense of smell," this term no longer seems adequate. The less commonly used word "savor," derived from the old French *sarur, savour*, meaning "taste," seems more appropriate, and we suggest its use in this sense.

Musk

Musk is a valuable and extraordinary odorant, which has been used since the most ancient times for its powerful, persistent and characteristic odor.

The different kinds of musk graded in decreasing order of quality are: Tonkin Musk grade I (the finest pods), grade II, grade III (small pods), Yunnan musk — musk from Assam — Saoko — Setchouen—musk from India or Nepal, Cabardine musk.

The assessment of a batch of musk is a delicate matter. The microscope can be used, alcoholic and aqueous solutions compared, and the odoriferous power estimated. High-grade pods should yield at least 70 per cent grain musk, while poor quality pods may only yield 40 to 60 per cent. The part which is soluble in strong alcohol represents 10 to 12 per cent by weight of the actual pods.

A number of products having an odor of musk are:

Natural Materials. Musk tincture, infusion, resinoid; Civet tincture, infusion and resinoid; Castoreum; Oils of Costus, Ambrette, Angelica Root and Seed, etc.

Synthetic products and specialties include Musk Xyol, Musk Ketone, Musk Ambrette, Exaltone, Exaltolide, Civettone, Thibettolide, Muscolactone, Ambrettolide, Hexadecanolide, Musk Carbonate, Musk Zibata, etc.

The two most recent, Phantolide and Versalide, are not macrocyclic musks, yet they possess the latters' main olfactory characteristics. *S.P.C.*

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ERTEL

(*Continued from page 107*)

ucts and packages, but every aspect of a company's dress, from offices, factory areas and lunchrooms through to trademarks and insignias, letterheads, trucks, shipping cartons and even uniforms of personnel.

The public today is becoming increasingly demanding of visual stimulation and increasingly responsive to it.

Maintenance of the status quo, or "things that look the same year after year," is no longer valuable in creating consumer identity. The public taste for change and stimulation is particularly evident in the color explosion we are seeing in cars, household appliances and home furnishings. In the packaging field, the sales success of packages that change and vary their illustrations frequently is another indicator.

Where companies have been outstandingly successful in exploiting their visual assets, they have used top notch design to express their own identities in a way that captures public interest.

Normal human beings receive better than 80 percent of all impressions of their environment through visual stimuli, so we are all strongly affected by visual change. Therefore, the visual potential inherent in most corporations is a neutral one that can be handled to create unfavorable as well as favorable impressions.

The designer, with his wide range of experience in influencing the public through visual means, is an indispensable adjunct to corporate efforts to convert their visual assets into good-will and sales.

"*In view of the many and obvious advantages of the Marlboro box, why was it necessary to spend valuable time and money researching its acceptability?*"
BURNS W. ROPER, PARTNER OF ELMOR ROPER AND ASSOCIATES

Now, in view of the Marlboro's sales success, as well as its obvious advantages, it does seem a little unnecessary to have researched its acceptability. But, at the time the Marlboro package was being considered, the filter market was relatively small, and was almost non-existent with men, partly because many men regarded it as affected to smoke filter cigarettes and as ostentatious to display them.

In light of this, there was considerable concern as to whether the stiff, hard box might constitute a barrier to sales, rather than a stimulant. Furthermore, history was strongly against a stiff box. With the exception of Parliament and one or two other brands, the whole trend has been away from boxes to soft packages.

Close to four hundred billion cigarettes a year were being sold in soft packages, and a large part of this volume was accounted for by brands that had abandoned hard boxes in favor of soft packages.

There was concern on the part of Philip Morris that people might be bothered by the inflexibility of

(*Continued on page 113*)

Trade Literature

Bulletin on Monopentek

Heyden Chemical Corporation, 342 Madison Avenue, New York, has issued a new technical bulletin on Monopentek, Heyden's monopentaerythrotol. The bulletin gives product data, including specifications, and summarizes the more important reactions.

Heyden has also published a new technical bulletin on Tripentek, Heyden's tripentaerithritol technical. The booklet gives properties and new uses, and reports on processing hints and resin formulations developed in Heyden's laboratories.

U.S.P. XV and N.F.X. Changes

An Abstract of Changes and Additions in the U.S.P.XV and N.F.X is available from Mallinckrodt Chemical Works at either 2nd and Mallinckrodt Streets, St. Louis 7, or P.O. Box 685, Church St. Station, New York 7. The booklet lists all products admitted to the U.S.P.XV and N.F.X, which became official last December 15. It lists all products that appeared in U.S.P.XV and N.F.IX but were not admitted to the new editions. In addition, it indicates products transferred from the U.S.P. to the N.F., and vice versa, and designates significant changes in products, titles, tests, and specifications.

Bulletins on Nacconates

National Aniline Division, Allied Chemical & Dye Corporation, 40 Rector Street, New York 6, has issued a series of six technical bulletins on Nacconates (diisocyanates) believed to contain the most comprehensive data so far made available on the properties and reactivity of this group of polyurethan chemicals.

Isopropyl Ether

Carbide and Carbon Chemicals Company, 30 E. 42 Street, New York 17, has issued a new technical bulletin (F-40003) which discusses isopropyl ether uses and contains up-to-date information on physical and physiological properties, specifications, and solubility and shipping data.

Aerosol News

Aerosol News, is a new house organ of the Kinetic Chemicals Division of E. I. du Pont de Nemours & Company, Wilmington 98, Delaware. The first issue, just issued last month, is dated Fall 1955. It will be issued quarterly.

Organic Chloride Compounds

Carbide and Carbon Chemicals Company, 30 E. 42 Street, New York 17, has issued a new 48-page booklet, Organic Chlorine Compounds (F-4769). Eighteen products, their applications, solvents properties, their handling and storage are discussed.

Carbide and Carbon Chemicals Company has also issued the 1956 edition of Physical Properties of Synthetic Organic Chemicals (F-6136). This 24-page edition features 32 new products available from Carbide and Carbon, and presents the latest data on more than 350 organic chemicals.

Carbide and Carbon Chemicals Company has, in addition, issued a new eight-page technical bulletin on epichlorhydrin (F-8862). Physical properties, applications, typical reactions, physiological properties, and references are presented in a convenient and concise form.

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are superior, non-greasy, non-sensitizing, liquid lanolin emollients containing 33% to 50% by weight of pure, *unfractionated* lanolin in oil-soluble form.

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Industry's Books...

Crop Protection, *by G. J. Rose, B.Sc., Entomologist (Micron Sprayers Limited), 223 pp., Illus., Philosophical Library, New York, (1955), Cloth,* **$10.**

This book is written for the cultivator faced with the problem of protecting his crops. It is a practical guide to the protection of crops from the initial seed stage to the stored product. In addition it is an aid to the planning of an intelligent program of measures for combating insect pests, fungus diseases, and competing weeds.

American Pharmacy, Textbook of Pharmaceutical Principles, Processes and Preparations, *Edited by Rufus A. Lyman, M.D., Dean Emeritus, College of Pharmacy, University of Nebraska, and Joseph B. Sprowls, Ph.D., Dean, School of Pharmacy, Temple University, Fourth Ed. (1955), J. B. Lippincott Co., Phila., 478 pp., Cloth,* **$9.75.**

This work is divided into two parts: Part 1—Metrology; Specific Gravity and Specific Volume; Heat and Refrigeration; Purification and Clarification; Mechanical Subdivision of Drugs; Solutions; Colloids, Emulsions and Suspensions; Extraction. Part 2—Waters; Syrups and Juices; Solutions, Injections and Sterile Suspensions; Infusions and Decoctions; Mucilages, Creams, Glycerogelations, Glycerites and Collodions; Mixtures, Suspensions, Magmas, Gels and Jellies; Emulsions; Soaps, Liniments, Lotions, Oleates and Sprays; Ointments, Cerates, Plasters and Cataplasma; Suppositories; Spirits and Elixirs; Vinegars, Tinctures, Fluidextracts, Fluidglycerates and Extracts; Resins and Oleoresins; Masses, Pills, Troches and Tablets; Powders, Capsules, Cachets, Oil-Sugars, Candy Medication and Triturations; Effervescent Salts; Radioactive Pharmaceuticals.

Industrial and Manufacturing Chemistry Part I — Organic, *by Geoffrey Martin, D.Sc., (Lond. and Bristol), Seventh Ed. Revised by Edward I. Cooke, M.A., B.Sc. 752 pp., Philosophical Library, Inc., New York, (1955), cloth,* **$17.50.**

In this edition the following old sections have been completely rewritten: "Mineral Oils and Lubricants"—"Condensed Milk and Milk Powders"—"The Fatty Acid Industry"—"The Illuminating Gas Industry"—"The Industry of Coal Tar Products." The following sections have been thoroughly revised: "The Sugar Industry"—"The Rubber Industry" and "The Industry of Modern Synthetic Drugs." Other sections have been brought up to date where possible.

Histamine, Its Role in Anaphylaxis and Allergy, *by M. Rocha E. Silva, M.D., Department of Biochemistry and Pharmacodynamics, Instituto Biologico, Sao Paulo, 248 pp., Charles C. Thomas — Publisher, Springfield, Ill., (1955), cloth,* **$7.50.**

The use of antihistamine drugs in the control of allergic diseases has renewed the interest in histamine. The clinical aspects of histamine, however, are only a by-product of Dr Rocha e Silva's considerations. The monograph presents histamine as a basic tool for the study of the mechanisms which are responsible for anaphylactic shock and sensitization diseases in man.

Plymouth

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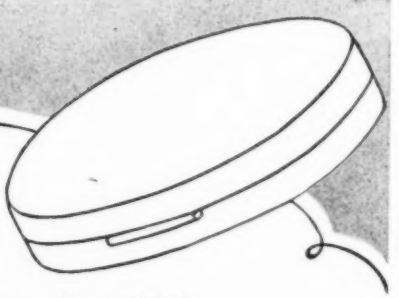

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(Continued from page 110)

the hard box—that it might be uncomfortable in men's shirt pockets; that it might not fit conveniently in women's handbags (although it has obvious advantages in handbags, too). And finally, there was concern over whether people would feel short-changed by the shorter-than-king-size length of the cigarette which the hard box necessitated. While these doubts may seem silly now, they were very real then.

It was because Philip Morris recognized the "many and obvious" advantages of the stiff box, that they undertook to research consumer acceptance of it—to determine which weighed more strongly with the consumer, the potential drawbacks or the potential advantages? The research resolved this question decisively, overwhelmingly in favor of the potential advantages. Thus the research served the purpose of permitting management to take what was then a risky gamble with a good deal of confidence. Without the research, they might have made the same decision, but, on the other hand, they might quite properly have felt that the risk was too great and that they should play it safe with the tried-and-true soft pack.

PRESS-COATED AND MULTI-LAYER TABLETS

(Continued from page 40)

weight control of each layer down to a variation of about one per cent or less; and third, a quality control check can be performed on each individual layer. The individual layer-compression method is, therefore, very useful for multi-layer tablet applications where extreme accuracy and good quality control are required.

Illustration No. 5 shows a multi-layer tablet press arranged to make accurate two-layer tablets by the individual layer-compression method. On this machine, two-layer tablets are made by filling the die with the first material and pressing it to make the first layer, then filling the die with the compressed first layer in it with the second material, and then pressing it again to form the finished two-layer tablet. Illustration No. 6. By adding an additional hopper, feed frame, and compression stage, a three-layer tablet machine would be obtained.

Quality control checks can be easily made while this machine is in operation. By pressing a lever, a sample first layer in the die can be automatically ejected while the machine is running so that the weight of this layer of material can be checked. If a three-layer tablet were being made by this method, a sample containing the pressed-together first and second layers could also be automatically ejected for a similar weight check. The weight of the final layer of material can be easily obtained by subtracting the weight of the first layer or the first two layers from the weight of the finished multi-layer tablet.

A practical multi-layer tablet press should have the following features:

POLAWAX is a non-ionic, self-emulsifying wax of the oil-in-water type and is an easily manipulated product giving extremely stable emulsions with all types of oils, waxes, strong electrolytes, chlorinated naphthalenes and similar chemicals. Send for booklet giving full details and suggested formulae.

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1. Clean separation between the various layers.
2. Accurate control of the weight and thickness of each layer.
3. Ability to sample check each individual layer as described above.
4. Ease of set-up and operation, with only one set of cams being required to produce a variety of multi-layer tablets. A press that requires special cams for each multi-layer tablet being produced is obviously limited in flexibility.
5. A three-layer press should also be able to make two-layer tablets and single-layer standard tablets when desired. In like manner, a two-layer press should also be able to make standard tablets when necessary.

To sum up, the new presses and techniques for making press-coated tablets and multi-layer tablets offer the pharmaceutical manufacturer additional tools to prepare and market new pharmaceutical products, or to modify and improve existing ones. One thing seems fairly certain at this time: Probably no two pharmaceutical manufacturers will use these two new types of special tabletting presses in exactly the same way.

THE INDUSTRY AND THE INVESTOR

(*Continued from page 25*)

foreign manufacturing plants being built by U.S. subsidiaries and international divisions, sales from which are not reflected in export data.

This change can be traced directly to foreign exchange restrictions imposed by most foreign countries after World War II. Rather than permit blocked funds to remain idle, American manufacturers used these profits for construction of factories and laboratories abroad. Among the advantages derived from this type of operation are lower labor and transportation costs and the establishment of better relationships between American companies and foreign nations.

Since the time a few generations ago, when barks, roots and herbs were the basis for most medicines and the discovery of a new major drug in twenty-five years was considered great progress, the role of the drug manufacturers has undergone radical alteration, and individual companies are still, more or less, in process of adjusting to the changing environment. Each company today maintains a large and costly research staff, the function of which is to protect the company's competitive position by developing a stream of new products, some of which may be useful. Most new products are marketed under brand names. Larger detailing staffs are now needed, not only to acquaint physicians with the merits of each drug, but to emphasize the company's brands.

Research and development expenditures are thought to average between four and five per cent of sales for most ethical drug manufacturers such as Schering with 10.8 per cent for 1954. Other manufacturers revealed the following research percentages for 1954:

Bristol-Myers 4.8 per cent; Merck & Co., 5.0 per cent; Park, Davis & Company, 4.1 per cent; Chas. Pfizer & Co., 4.2 per cent; Smith, Kline & French Laboratories, 5.0 per cent; and Warner-Lambert, 2.1 per cent. Research expenditures of Abbott Laboratories is estimated at 4.0 of sales by Standard & Poor's, and those of Norwich Pharmacal Company are estimated at 3.4 per cent of sales.

Comparisons in terms of percentage of sales are not too reliable since most firms are not engaged exclusively in the ethical field, where research outlays run from two to three times those in the proprietary field. In addition, companies with sizable overseas business tend to spend less than companies conducting a relatively small foreign business. Since products sold abroad are the same as those sold in domestic markets, these companies have no need for duplicating research work.

Chemotherapy dates back to the late nineteenth century. One of the earliest drugs developed was Salvarsan (1909). Aspirin is another of the precursors of modern methods. Sulfa drugs, introduced in the late 1930's, began the rapid strides made toward the conquest of infection.

Discovery of the antagonism between molds and bacteria was first announced in 1897, but it remained for the World War II emergency to develop mass production of a practical product, penicillin, which was first available in 1942. There followed in rapid succession streptomycin (1944), Aureomycin (1948). Chloromycetin (1949), Terramycin (1950), Erythromycin (1952), and Tetracycline (1953). Many additional antibiotics have been announced, but these are used largely in specific cases, and in instances where the bacteria is one that is resistant to the older drugs. Thus far, no antibiotics have been developed that are effective against many viral diseases such as colds, grippe, influenza, encephalitis, measles, mumps, and smallpox. Therein lies a fertile field for research.

The use of antibiotics has been so effective that tuberculosis and pneumonia formerly the number one and two killers in this country, have given way to heart disease and cancer. The Metropolitan Life Insurance Company reported that, in 1954, nearly three-quarters of the amounts paid to beneficiaries were for deaths caused by diseases of the heart or blood vessels, or by cancer. Twenty-five years ago, the proportion was only 31 per cent.

Use of hormones in therapy probably began during the 1920's with distribution in this country of products under foreign patents. They consisted mostly of several varieties of sex hormones. Compound E, cortisone, was isolated in 1935 from the adrenals of cattle, and is now synthesized from abundant raw materials. Found effective against arthritis, rheumatic fever, asthma, certain skin and eye conditions, and many other ailments, cortisone, and its companion product hydrocortisone had adverse side effects which resulted in the discovery early this year of prednisone and prednisolone. These later products,

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It owes its popularity, according to one recognized authority,* to a combination of at least three qualities: it is non-toxic, protective and mildly astringent.

* *The Dispensatory of the United States of America, 1950 Edition*

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Products Distributed by
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more effective and with greatly lessened side effects, are believed to account for well over 25 per cent of the improvement in ethical sales in 1955.

The trend in sales of both ethical and proprietary products has been upward, with ethicals showing the sharper rise. The decline in dollar sales of ethical drugs subsequent to 1951 reflected the collapse in penicillin prices and lower prices on other antibiotics.

The population of the United States is expanding rapidly, and an increasing proportion is falling into the older age categories. The incidence of disease and disabling afflictions is greatest in the over-55 age group, and it is in the treatment of just these diseases —hypertension, cancer, cardiovascular disorders, and degenerative ailments—that the medical profession has been least successful in spite of the progress made.

With 750,000 people in the U.S. in mental hospitals, and several times that number of mentally ill in a non-hospitalized status, the potential is great for drugs to combat mental disorders. Rapid strides have been made since 1953, including the introduction of reserpine and chlorpromazine, but this market continues to offer one of the best possibilities for expansion of the drug industry.

A.P.M.A. MEETING

(Continued from page 27)

sion by *T. J. Tsevdos*. Press-coating, by which granulated powder is compressed around a central core tablet, producing a tablet-within-a-tablet, permits many new interesting combinations. For example, two incompatible materials can be combined in a single tablet; a heavy time-delay or enteric coating can be applied to the core tablet; a material (such as aspirin, penicillin, etc.) which is damaged by water and hence cannot be coated by the conventional pan-coating process, which requires water to be present, can be dry-coated; and tablets can be made which contain double and even triple dosages. Press-coating also permits the finished dry-coated tablet to be marked with the manufacturer's trademark, which cannot be done with pan-coating, and also provides an attractive means for reducing or eliminating the time and the labor cost involved in pan-coating operations.

Multi-layer tablets are now being explored by the pharmaceutical industry thanks to recent developments in tabletting machinery that provide the necessary accuracy and provisions for quality-control checking. Typical applications being considered, include three-layer tablets of two active materials separated by a middle layer of inert material, combinations of two or three incompatible materials in separate layers, and tablets with multi-colored layers for better product-identification.

Mr. Tsevdos also described in detail several new types of tabletting machines developed by firms like Stokes, which enable these new combinations to be made economically and with good control over the weight and density of the finished tablets.

Three papers were presented on the general subject of "Drug Therapy in Mental Disease." *Dr. B. L. Keyes* discussed **Psychiatric Perspectives.**

During the past 50 years, an extraordinary change has taken place. Asylums have become fully staffed and equipped hospitals. Physical aspects of mental disease and mental disease in physical conditions have been explored with great intensity. Bacteriological diseases and their controls have been established. Surgical procedures on the brain for certain forms of chronic mental illness have been devised. The use of sedative, hypnotic, anti-spasmodic and anti-convulsive drugs have become established practice.

Modern technical facilities have made it possible to greatly shorten many psychiatric illnesses and to cure many cases once thought to be hopelessly chronic. By 1950, for example, an 80 per cent recovery rate for cases of acute schizophrenia had become the accepted expectancy. Since the control of syphilis by penicillin, general paresis has all but disappeared.

More recently, the chemotherapeutic investigations have been directed toward distinct clinical entities, particularly toward certain groups of symptoms. Newer drugs now invite us to subdue difficult and disturbed patients by the simplest of means. We are steadily moving away from the more radical measures of recent years and gratefully accepting the promise of simplified therapeutic agents which may soon not only aid us in controlling symptoms but may lead to the very core of the illness we have found so difficult.

Dr. F. J. O' Neil evaluated **Tranquilizing Drugs.** Twenty-five years ago, custodial care was about all that could be offered to the patient suffering from a severe emotional illness. Since then, significant changes have been made in the care and treatment of the mentally ill. Insulin coma treatment for schizophrenia provided the first hope for this chronic, regressive disease. Electro convulsive therapy has materially affected the treatment of the depressive types of mental reactions. The introduction of psychosurgery offered a new approach to the treatment of the major psychoses. Yet none of these materially influenced either the rate of admission to mental hospitals, or significantly reduced our mental hospital population. Since 1909, the rate of admission per 100,000 of population for mental hospitals of New York State has increased from 65.1 to 132.0 or, over 100 per cent increase in less than 50 years. Approximately one out of every ten dollars raised by the State of New York by taxes is required to provide care for the mentally ill.

During the past eighteen months, we have entered a new phase in the treatment of mental illness. This may well be referred to as the era of Chemopsychiatry, for the introduction of the tranquilizing drugs may revolutionize our concept of the care and treatment of the mentally ill.

Although it is too early to predict the total effect of these drugs on our psychiatric patients, they have

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produced improvement in the conduct of the disturbed patient, and, therefore, the atmosphere of the disturbed ward. Their wide use has made it possible to care for the aggressive, regressed patient in a more wholesome environment that more closely resembles the hospital atmosphere of the rest of the institution. There is no doubt that this change has greatly improved the morale of the ward employee and has encouraged him to work more diligently to promote the recovery of the patient. These drugs have also provided the means for abating the distressing delusional and hallucinatory symptoms usually seen in the early schizophrenic patient.

During 1955, while these drugs have been extensively used in New York State mental hospitals, there has been a pronounced improvement in the patient release rate. Whether this will be sustained, cannot be predicted. The records of the New York State Department of Mental Hygiene show that since the latter part of 1953, there has been a steady decline in the state wide employment of psychosurgery in the state mental hospitals. Electro convulsive therapy has shown a marked decline. There has also been a marked reduction in the application of restraint in the care of mental patients.

The fact that we can now successfully treat mental symptoms with chemical agents reaffirms our belief that psychiatry is a branch of medical science and should be closely allied with other medical specialties. The full impact of these new drugs has not yet been adequately measured, and our attitude should be skeptical yet optimistic.

Dr. H. D. Fabing discussed **The New Pharmacologic Attack in Psychiatry.** Many hallucinogenic drugs being studied at present belong to a group of compounds common to biology called indoles. The indoles are not all hallucinogenic for man, however. They raise a tantalizing thought that schizophrenia may be a biochemical disease, a disease of metabolic error caused by the production of abnormal indoles in the body which poison the brain and produce the clinical picture of schizophrenia. This group of drugs under study include mescaline and its derivatives, the metabolites of adrenalin and reserpine. Two different tranquilizing agents under recent study are chlorpromazine and a piperidyl compound.

The advent of mephenesin in England ten years showed that drugs which were not sedative could lessen the symptoms of tension and jitteryness which engulf the patient sick with an anxiety reaction. A mephenesin derivative recently made available, will be used by general practitioners in one of every four or five patients who come through his door if it will relieve anxiety symptoms, for this is one of the most common ills of man.

Although the new pharmacologic attack in psychiatry and in neurology is imposing in its accomplishments in recent years, only a beginning has been made. The areas of ignorance are so vast that this is still a frontier.

T.G.A. SCIENTIFIC SECTION MEETING

(Continued from page 31)

This is time-consuming as well as expensive. Thus, a need existed for a simple *in vitro* test which would reasonably forecast the results of the Cade Handwashing Test. This need resulted in the development of the Protein Adsorption Test which consists of washing ordinary cleared photographic film with a test soap composition, followed by evaluating the washed film for adsorbed and active antibacterial agent by use of an agar plate test. The Protein Adsorption Test permits the rapid selection of promising antibacterial agents from the many that are presented for screening.

In the final paper of the session **A Practical Approach to Container Development for Toiletries** was discussed by *A. R. Jasula*. Containers can be plus factors or pitfalls in the marketing of toiletry products. It is important that the evaluation, and choice of containers be carried out in a practical and scientific way. Considerations which deserve study and research include eye appeal protection and preservation; utility and function; costs; regulations and safety; operations at the filling plant.

The paper elaborated on these considerations and discussed how they are studied. It stressed the necessity of studying all considerations rather than just one or some. There was a dissertation on facilities and personnel for container development. Climate rooms, physical "beater-uppers," examining and measuring apparatus, corrosiont esting equipment and other specialized equipment were included in the paper's scope. Requisites for personnel were given.

SOCIETY OF COSMETIC CHEMISTS MEETING

(Continued from page 35)

the potential utility of such materials as active ingredients in anti-perspirant-deodorant combinations was reviewed. For example, the selectivity of certain resins for fatty acids, ammonia, and other products of apocrine sweat were outlined. Information was supplied on the deodorizing properties of certain resin adsorbents as judged by laboratory and clinical studies. From these data and from the knowledge of the properties of various ion exchange materials, proposals were offered on the ideal type of synthetic adsorbent for antiperspirant-deodorant formulations.

Finally, the utility of these exchangers in other dermatological applications were briefly outlined.

V. K. Babayan presented his paper **Fatty Acids and Derivatives in Cosmetics.** Fatty acids are used as building blocks to synthesize derivatives having specific physical and chemical properties for varied industrial uses. Chemical composition as well as the specific orientation and/or configuration of a given fatty molecule plays a major role in the properties of these synthesized esters.

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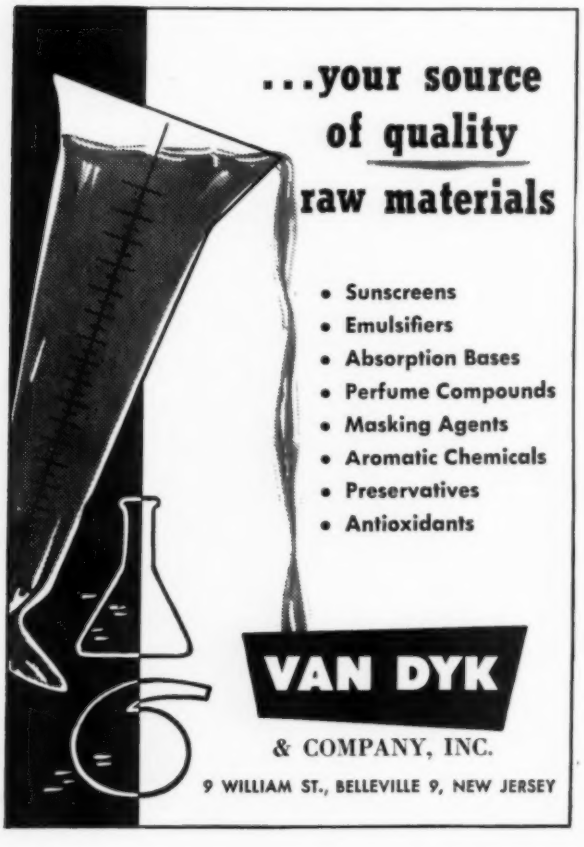

Hard Butters manufactured by various techniques were described and compared to cocoa butter, demonstrating the flexibility and versatility of the tailor-made products over the naturally occurring fat. Oils of exceptional oxidative stability, fluidity at sub zero temperatures and even alcohol solubility in combination with the other desired characteristics can be achieved in fatty esters, illustrating the broad range of possibilities that exists in a field that is looked upon with passive interest.

J. V. Klauder presented his **Review of Dandruff Research to Date.**

Probably no common disorder of the skin has been subjected to more controversy than dandruff. The controversy particularly concerns what role several organisms, especially Pityrosporum ovale plays in its cause; the complexity of terms employed in its designation; the relation of dandruff to seborrhea and to baldness.

Pityrosporum ovale and what role it plays in causing dandruff was discussed as well as the modern concept of dandruff and seborrheic disorders. It is difficult to separate dandruff in discussion of the seborrheic state and its disorders. Hormonal influence, dietary and other influences, vitamin deficiency, estrogenic creams were also touched upon.

Time-honored preparations in treatment of dandruff were reviewed and their mechanism of beneficial action discussed.

Newer remedies in treatment of dandruff embrace—(a) conventional long-used ingredients, (b) preparations allied to sulfur, selenium and tellurium, (c) quaternary ammonium compounds, (d) fungicides, (e) vitamin B components.

A method of evaluating efficacy of anti-dandruff preparations was presented and suggestions regarding formulation of new preparations in treatment of dandruff were discussed.

Etiology and clinical aspects of *seborrhea capitis* (dandruff) and *seborrheic dermatitis* of the scalp and other areas of the skin discussed by *A. H. Gould* in his paper **Sodium Sulfacetamide.** Evolution of medical terminologies categorizing the various stages of seborrhea as well as the role of micro-organisms as possible contributors to seborrheic eruptions were presented. The clinical picture—developmental stages and pathological manifestations of *seborrhea capitis* and *seborrheic dermatitis*—were described. Favorable clinical results obtained with sodium sulfacetamide used topically in the treatment of a large group of patients with *seborrhea capitis, seborrheic dermatitis,* or *bacterial cutaneous infections* were reported.

E. J. Matson presented his paper **Selenium Sulfide an Anti-Dandruff Agent.**

Selenium sulfide, because of its close relationship to sulfur, has been for many years considered a possible agent for the treatment of dermatoses. It was finally found that an effective agent could be formulated by combining selenium sulfide with a hydrophilic agent and a detergent. This preparation, known as Selsun,

controls a high percentage of cases of seborrheic dermatitis of the scalp, of which dandruff is a mild form, and of other areas such as the eyelid, nasolabial fold, and external ear canal. In a somewhat different form, known as Seleen, it is highly effective in certain nonspecific dermatoses of cats and dogs, and in the control of dermodectic mange.

Just as the etiology of dandruff has not been established, so the actual mode of action of the selenium sulfide preparation is not known. Little evidence in recent years has been gathered to support the theory that dandruff is caused by the fungus *Pityrosporum orale*. However, selenium sulfide suspensions have antifungal activity.

It has been suggested that selenium activates sulfur, and that it is the sulfur which is the effective antidandruff agent. This is an interesting theory. However, the action of selenium sulfide is not entirely that of elemental sulfur. In some patients treatment is followed by an increased oiliness of the skin, which does not occur with sulfur alone. As a result of this observation it has been suggested that selenium sulfide may act by correcting an abnormal skin fat condition.

Investigators have demonstrated a twofold effect of Selsun on sulfhydryl groups in human epidermis; the detergent releases previously non-reactive sulfhydryl groups, some of which are then inactivated by selenium sulfide. It is possible that these effects are related to the repression of scale formation in dandruff.

THE PHARMACEUTICAL INDUSTRY AND HEALTH

(Continued from page 37)

tant than a good bedside manner, pure science is more valuable than applied, the laboratory worker ismore useful than the executive, the clinical investigator contributes more than the pharmaceutical manufacturer. All these are important in their own right. The significant thing is that these and many others complement one another, and, as members of the health team, the role of each one of them is essential to medical progress.

These spectacular gains have been achieved through the collaboration of the medical profession and its basic sciences and the pharmaceutical industry.

In no other field of endeavor has this kind of partnership been more productive of good for mankind. In all of history it is one of the brightest chapters of industry and a profession working together to their mutual interest and for the common good.

But our job has just begun. There are still bacteria that haven't been mastered, and it is likely that the appearance of new mutants will keep us busy in this field for a long time. Although the conquest of one of the meanest diseases of them all—poliomyelitis—now appears within sight, there is still a

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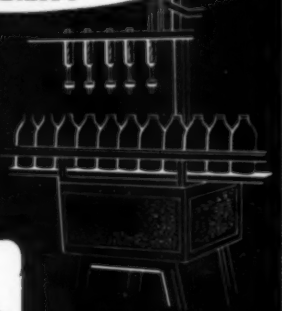

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whole host of virus diseases that are as yet untouched. Cancer is still a who-done-it mystery to which there is not a single basic clue. We have a good palliative for diabetes but we still don't understand the basic pathogenesis of this disease. A whole host of endocrine, mental and neurological disturbances still defy our best research brains. Arteriosclerosis, the greatest killer of them all, and the ultimate limiting factor in our life span, is still beyond our grasp. There is no doubt that our scientists have plenty left to do, and so long as mother nature fails to create and maintain perfectly functioning bodies, she will need the combined research help of our physicians and the pharmaceutical industry. But the most significant and encouraging aspect of medicine today is the fact that at long last we have learned how to go about picking the lock of nature's hidden secrets.

Opening these doors is not a one man job. In the future, more than has been the case in the past, new discoveries will emerge as the culmination of the combined efforts of many workers covering the scientific spectrum from physics and chemistry to clinical medicine.

One over-riding problem of medicine, the importance of which cannot be over emphasized, is that the public has a deeply ingrained impression that medical care and the drugs that are a part of it, cost too much. This is the basis of the most serious threat to the practice of medicine as we know it. It is a challenge to free enterprise in the practice of pharmacy and the manufacture of drugs. Public attitudes respecting the cost of medical care and drug prices can, over the long pull, substantially alter public attitudes about socialized medicine.

Today a few pills costing perhaps several dollars are often the equivalent of what used to be a perilous illness with long disability, loss of earnings, hospital and nursing expense and a convalescence that sometimes lasted for months.

For instance, Dr. Ivor Griffith made a study of the cost of a case of pneumonia in a Philadelphia hospital in 1927. He found that the average hospital, doctors', and nurses' bill amounted to $358.00 and the duration of hospitalization averaged five weeks. During this time and a subsequent convalescent period, the loss of earnings brought the total cost of the illness up to approximately $1,000—and that was when a thousand dollars really was a thousand dollars. I can add that in 1953 the average duration of lobar pneumonia was less than two weeks with no period of convalescence required. Most cases were treated at home with antibiotics costing the patient approximately $15.12 if penicillin was used and $29.68 if one of the broad spectrum antibiotics was employed. While we have no comparable figures for loss of earnings it is nevertheless evident that a great economic saving has been achieved. Added to this is the fact that many potential cases never get to be full blown pneumonia because of the prompt use of antibiotics.

Most important of all is the fact that the undertaker used to get one good funeral out of every five cases of lobar pneumonia whereas today we have deprived him of almost all of this business.

Perhaps it just isn't human nature to feel deeply grateful for having been spared a perilous illness that everyone knew wasn't going to happen. In the old days when patients were snatched from death's door after a period of mortal peril and suffering, there was less complaint about the cost of medical care.

There are some 40 million cars on the road. Today people are perfectly cheerful about spending $2,500 to $5,000 to replace cars that we know from World War II experience are good for several more years of service. And yet those same people cry to high Heaven if they are charged a small fraction of that amount for the medical services that may save their very lives or at least make it possible for life to be worth living.

Drug prices have advanced far less than that of most other commodities during the past 15 years of inflationary pressures. Actually the percentage of Disposable Personal Income spent for medical care which includes drugs, has remained practically constant for 20 years at about four per cent. The low value of 3.9 per cent occurred in 1935, the highest proportion—only 4.2 per cent—in 1954, due principally to the markedly greater expenditure for hospitalization and medical care insurance. The public spends far less for medicines than it thinks. In 1954, the per capita consumption of drug preparations and sundries was $10.00. Imagine, just $10.00 a year, on the average, to keep well and to prolong life! How does this expenditure compare with others about which the public remains silent? Here are the per capita expenditures in 1954 for a few other products and services:

Alcoholic beverages	$54.00
Tobacco products	$32.00
Interest on personal debt	$18.00
Auto repair, greasing, washing, parking, storage, and rental	$18.00
Admissions to specified spectator amusements	$11.00

And here is a comparison that should make us wince. Whereas personal consumption expenditures in 1954 for drug preparations and sundries amounted to $1,631,000,000, death expenses (funeral and burial service, cemeteries and crematories, monuments and tombstones) cost the American people $1,162,000,000. We spend not much less to bury our dead than we do to stay alive—but we seem to object to the cost of staying alive.

The statistics I have here cited are official figures. Authority for them is the U.S. Department of Commerce. These figures, if generally known to the public, could produce a vast change in its opinion concerning the cost of medicines. Yet they do not tell the whole story. They say nothing of the savings in health and in hard dollars which the American people have made by virtue of the contributions of scientific research.

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Indeed, I would venture the guess that the advances in therapeutic agents and in medical care during the past decade alone account for far greater economic gain than is represented by the total cost of medicines today.

FLAVOR ANALYSIS

(Continued from page 29)

base judgment of a flavor. In this respect, it would be very useful to the people who approve products for marketing, because the product's flavor characteristics can be seen at a glance on a tabular flavor profile. Another service the profile performs is in showing the project leader where he stands in respect to the flavor formulation development. According to people who are using flavor testing programs, panels serve as inspiration to the researcher in charge of flavor formulation. And by the same token, profiles could serve in the same way because they show the researcher what sort of progress he is making and provide a basis on which to judge the direction of the program.

A flavor profile can also serve as a standard or control (because it is reproducible). In this way it facilitates screening of raw materials and checking flavor stability. Samples kept at room temperature or that are refrigerated usually serve as controls, but even under these conditions the flavor can change. And at times a new flavor would have to be made up. A flavor profile standard would eliminate this. In its role as a standard or control, the flavor profile also serves well in setting up taste and odor standards and specifications. (In the paper and electrical appliance industries, for example, the profile has been used successfully in setting up specs.) It is particularly adaptable to this application because of its encompassing nature.

Requisites for Panel Operation

Flavor testing programs are finding increasing application, and are gradually being introduced to more and more companies. It is of prime importance that panels be conducted without undue interference or pressure, because panels must be as free of distractions as possible if they are to function well. Panels must have confidence in themselves, and if they do not feel that their work is significant and if they are not given adequate time for the taste testing, they cannot be expected to operate effectively.

Screening and training of panel members is another requisite. A flavor panel should be composed of people with normal ability to taste and smell (it is neither necessary nor even desirable to have people with hyper-acute senses). They also should have a high degree of interest in flavor; given sufficient enthusiasm, almost all people can be trained to become effective panel members.

Training, of course, is necessary for an analytical panel to operate efficiently. But during the training period, the panel is still useful. It is simply a matter of guided experience and practice.

In using profile panels on pharmaceuticals, ADL has found several basic procedures in flavor correction. For example, in materials that coat the mouth but that cannot be diluted in preparation, salivating agents such as monosodium glutamate, salines, dilute acids, and essential oils can be tried. Another approach in flavor correction is to incorporate one or more taste factors into the product; sweeteners and monosodium glutamate often counteract bitterness; edible sequestering agents will sometimes reduce the metallic character of hematinics; bitters and salt can reduce cloying sweetness; and salt and sugar—separately and together—can be added to combat sourness. Raising the level of all primary factors together may produce a desirable effect.

An undesirable odor factor frequently yields to other aromatic factors and becomes a hidden part of a bouquet. This blending is also helpful in ameliorating unpleasant flavor factors. By their very nature the aromatic syrups and elixirs are bound to be useful vehicles. Containing at least one taste factor, several aromatics, and usually a feeling factor, syrups may influence each of the three basic aspects of flavor. But these vehicles are not necessarily interchangeable. One that is useful in eliminating an extremely sour taste would probably be found lacking for fishy flavor. The flavorist will have to develop the vehicle according to the flavor pattern of his problem. Perhaps the optimum procedure is first to blend out or reduce the unwanted flavor factor and then add a flavoring to give the preparation a pleasing taste.

Regardless of the technique used, a flavor panel is a practical aid in charting progress and pointing the direction to ultimate correction and appeal. Flavor analysis is finding increasing use, and those interested in achieving and maintaining high-quality flavor find this simple tool indispensable. It is a compass that can be used to advantage in the pharmaceutical industry of today and tomorrow.

THE NEW PHARMACOLOGIC ATTACK IN PSYCHIATRY

(Continued from page 33)

metabolic error, a disease caused by the production of abnormal indoles in the bodies of people—indoles which poison the brain and thereby produce the clinical picture of schizophrenia? It is only a thought, but as the evidence mounts, it becomes a more respectable thought, worthy of the most intensive research effort. If a mechanism such as this can be established, specific drug therapy cannot be far off. The stakes are high. The making of productive citizens—taxpayers instead of tax spenders—out of this large mass of cruelly afflicted patients would probably go down as one of the greatest triumphs of the 20th century for the medical and pharmaceutical professions.

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quainted. Reserpine, of course, comes out of herbal medicine, the herbal medicine of the Orient. This very complex compound is, of all things, an indole. Its basic structure is similar to that of yohimbine, one of the hallucinogens. Reserpine is yohimbine with a complex phenolic radical attached to its tail. Under certain experimental conditions it is a serotonin antagonist, and some people believe that this is the way it acts.

It has produced some excellent therapeutic effects in chronically ill patients in mental hospitals. The studies of Kline at Rockland State Hospital in New York, and of Pennington in Mississippi are especially encouraging. Large doses of the drug are necessary to bring about these effects.

In office practice, about which I know something, the side-reactions of reserpine often lead one to defeat. Despite careful forewarning of patients about nasal stuffiness, drowsiness and dizziness, when these things begin to occur the telephone almost jangles off the hook. On the next visit the patient often reports that he gave it up because of its unpleasantness. Blood pressures can fall quite low with this drug, and must be watched carefully. Perhaps the most difficult complication encountered with it is the mental depression it can produce. My colleagues and I have been concerned about this, as have other clinicians, and we have had to resort to electroshock therapy on occasion to circumvent it. Despite these difficulties, reserpine has found a real place in therapy in psychiatry.

Chlorpromazine, the Rhone-Polenc discovery, has had a very wide use in the past two or three years. One of the most earnest students of this drug is a colleague of mine in Cincinnati, Dr. Douglas Goldman. He is the medical director of a very large, overcrowded, understaffed state institution, Longview Hospital. He has taken a new lease on life lately. The reduction in assaults, the lessened use of restraint, the increased granting of privileges to locked-ward patients, the lessened need for repeated electroshock treatment to control explosive behavior, and the beginnings of an improved discharge rate of patients from the hospital all stem from the use of this drug in his hands, and parallel the kind of improved state of affairs which Kline reports with reserpine at Rockland.

Goldman likes to tell the story about Willie. Willie was a dishevilled, mute, untidy schizophrenic who had to be spoon-fed and who managed to tear off just about all the clothes anyone tried to put on him. Willie received an eight weeks' trial with chlorpromazine, but at the end of that time Goldman was not greatly impressed with his improvement. He announced that he was going to withdraw Willie's drug, whereupon an orderly raised a clamor, pleading for its continuance, insisting that Willie was much better. He said, "Wait a minute. I'll prove it to you. I'll get Johnny." In a moment he returned with Willie's identical twin. "See, they were both alike two months ago," he said. They stood side by side. Johnny's hair fell in his face,

he was soiled, his pants were torn, and he was barefoot. Willie was fully clothed, barbered, shaved, clean, and wore shoes. The difference was obvious. Instead of taking a patient off chlorpromazine, he put another on.

Again, in office practice this drug is harder to manage than in a hospital setting. The complications of skin rash, drowsiness, dizziness, apathy, jaundice and parkinsonism, among others, tend to discourage some patients and their families from its use. Again, mental depression has a way of arising on occasion. This requires electroconvulsive treatment if mere withdrawal of the drug does not alleviate it. Despite these things this, too, is a heartening new therapeutic tool which we have welcomed gladly. The mode of action of this compound has defied explanation. If this were known, it seems plausible that other congeners of chlorpromazine, having fewer side-reactions and greater efficacy, could be synthesized and applied.

For the past 18 months we have been worrying along with another of the tranquilizing drugs, or ataraxics, as I have called them. This word comes from the Greek, *ataraxia*, which means *freedom from confusion* or *peace of mind*, or *detached serenity*, as Ivan Bennett has translated it. For one like myself who has lived for a score of years through all kinds of therapeutic attempts in psychiatry, these drugs have constituted a new order of experience, so different have they been from anything in the past. I felt that we needed a new word to encompass their action, and thus comes the term "ataraxics."

The other ataraxic is Frenquel, a product of the Merrell Company. This compound is a piperidyl, and one is hard put to imagine how it can act effectively on a muddled brain when one looks at its formula. The only small contribution I can make is that the piperidyls are found in peppers, the spices over which many a war has been fought because they are so highly prized. The Indian of the Americas lives on a diet of corn, which is a good way to get pellagra, a disease which often has schizophrenic manifestations. But the Indians don't get pellagra. They eat peppers with their corn. Do the piperidyls they get with their diet keep them sane? I am sure that I don't know. I throw the idea in for what it is worth.

Frenquel is an exasperating in-and-outer. In some acute schizophrenic syndromes—about 40 per cent of them—it has been dramatic in its efficacy. It has been less valuable in the chronic cases. We have found that it will block the development of an LSD or a mescaline psychosis when given as a premedication in a small number of experiments, and will abort these reactions when given intravenously. Some investigators have confirmed this, whereas others do not agree. A larger number of experiments will probably prove that Frenquel has this blocking effect in some cases but not in all of them.

One day while I was sitting in my father-in-law's hospital room 48 hours after he had undergone a prostatectomy. I had just come downstairs from where we had been doing a mescaline experiment.

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Suddenly I realized that my father-in-law was talking just like the mescaline subject had been doing upstairs. He was disoriented, confused, frightened and hallucinated. He had sensations of levitation as though he and his bed were slowly swinging through space, and he complained of being bitterly cold. His post-operative confusion became worse as I sat there, and when he tried to climb out of bed and pull out his catheter, I realized that something had to be done. It was so like the mescaline reaction! Why not try Frenquel? I gave him 50 mg. of the drug intravenously and watched his psychosis melt away during the next half hour.

This has launched us on an inquiry into post-operative psychoses. Frenquel has been almost uniformly good in relieving approximately 75 cases of this type. Other confusional states respond nicely, too. After having dramatic success with two cases of delirium tremens we looked for others but could not find them. Apparently they have worse whiskey in North Carolina. Proctor at the Bowman-Gray School of Medicine in Winston-Salem has relieved 16 of 19 cases of delirium tremens quickly with Frenquel. Senile patients often go through troublesome confusional periods. Frenquel has helped us with these on many occasions, too. Our best friends in this have been the nurses. They run a quieter hospital and require less restraint for disturbed patients. We are enjoying a popularity with them which we never had before. One nice advantage of this drug is that it produces no side-reactions.

This brings us to a consideration of another group of new compounds which act on the central nervous system—the cerebral stimulants or euphoriants. Alcohol is the most widely used of these, but as you will find at your office Christmas party which is coming up (if you have never noted it before) it is completely unreliable in its effects. Rather than stimulate, it depresses some brains and makes others wild. Cannabis, mescaline and bufotenine-containing mushrooms have all been used for the same purpose, and are equally unpredictable. They just won't do in therapeutics.

The advent of the amphetamines marked a new step in the search for mood-elevating drugs, and they they have won a real place for themselves in therapy. For the past three years we have been studying one of the precursors of Frenquel, another piperidyl compound, Meratran, a Merrell product. It has an action similar to the amphetamines, but does not produce appetite loss as they do, and does not affect blood pressure and pulse as they do. Ritalin, another compound of this family, developed by Ciba, has similar properties. It was our hope in the beginning that these drugs would provide us with a new method of attack in melancholia, but they have fallen short of the mark.

In all the talk about schizophrenia which is going around, the other great functional psychosis, melancholia, has been lost in the shuffle. This shouldn't be. Although schizophrenia is a far more chronic disease, and although it fills more long-term hospital beds, melancholia is a more common disorder. My associates and I, who meet all comers, and who can best be described as general practitioners of disorders of the nervous system, encompassing the fields of neurology and psychiatry as we do, find that we encounter at least four or five new cases of melancholia for every one of schizophrenia in our consulting rooms. I have never gotten used to this disorder. I am just as amazed at a case I saw last week as those I saw as a student. Why or how can a normal hard-working, God-loving man or woman suddenly be thrown into a state of disturbed sleep and disordered mood which is completely disabling? I have seen this happen between a Tuesday and a Thursday. These people suddenly lose their power to concentrate their minds on the simplest activity such as reading the evening newspaper, they find all social intercourse painful and give up their friends, they believe that they are burdens on their loved ones, they develop the most illogical feelings of guilt and sin, and they quit eating. Unless something is done about them, suicide occurs all too frequently. I am just old enough to remember this torturing disorder before the shock therapies were introduced. Patients and their families crawled through months and even years waiting for the *vis medicatrix naturae*, the curative power of nature, to put these depressed minds back on the normal track again. Electroshock therapy has compressed these attacks into a matter of a few weeks, and depressed patients seldom gravitate to the back wards of state hospitals any more. But they are still with us, and although electroshock therapy is a blessing for most of them, the patients, their families and their doctors have never really liked this form of treatment. There is something assaultive and violent about it, try as we do to improve our techniques of administering it.

There is surely something which goes awry in a patient's body chemistry in this strange illness. Some of my colleagues insist that it is psychogenic—that we humans worry and think ourselves into melancholia. This becomes harder to accept as the continuing parade of these patients passes in review before us. We have been forced into inventing words to hide our ignorance about the etiology of this disorder. We say that a great number of these cases are endogenous—that they come from within, which is another way of saying that something goes wrong in the chemical brew within us to produce these states. Here, if anywhere, is a challenge of the first magnitude for the neurochemists and the neuropharmacologists. I, personally, will give a gold medal to the man who solves this riddle.

Before I close this discussion, a word should be said about the new attack on anxiety neurosis and on epilepsy. The advent of mephensein in England some ten years ago heralded the fact that drugs which were not sedative could lessen the symptoms of tension and jitteryness which engulf the patient sick with an

anxiety reaction. Mephenesin, too, has been an in-and-outer, and only helps in a fraction of the cases in which it is used. Recently a mephenesin derivative, called Miltown by Wallace, and Equanil by Wyeth, has been made available to the clinician. The votes are not in from all the precincts, but some of the early returns are most hopeful. If this drug or others like it will relieve anxiety symptoms, it will be used by general practitioners in one of every four or five patients who come through his door, because this is one of the most common ills of man. Let us hope and pray.

The researches of Merritt and Putnam which led to the introduction of Dilantin by Parke-Davis in 1937 have had an impact on a million and a half people with epilepsy in this country and untold others throughout the civilized world. Like many of the drugs used in nervous system disorders, it has its drawbacks and its disappointments, but it was a monumental stride forward. Here is an example where the invention of a new pharmacologic tool opened up new therapeutic vistas. It arose out of the discovery by two Italians that fits could be induced in cats by passing an electric current through their heads. Merritt and Putnam tested the ability of seven hundred compounds to inhibit such fits, and Dilantin is the result. Here, again, is an example of the tenacity of the pharmaceutical industry. Dilantin was good, but not perfect. The continuing efforts of other companies, Sandoz with Mesantoin, Imperial Chemicals with Mysoline, Parke-Davis with Milontin, Lederle with Hibicon, and the long-term effort of Abbott which has yielded Tridione, Paradione, Phenurone, Gemonil, and now Peganone (which seems to be the best of their group of compounds according to preliminary report) has converted the epileptic from a second-class citizen to a first-class one in this country, and is permitting him to cast aside the stigma which has surrounded his illness since Biblical times. The epilepsy story during the last 20 years is one of the most creditable achievements of your industry, and you deserve an orchid for it, especially if you don't quit now that the battle is being won.

The new pharmacologic attack in psychiatry and in neurology is imposing in its accomplishments in recent years. I am sure that you will all agree that much remains to be done—that only a beginning has been made. The areas of ignorance are so vast that this is still a frontier. It is anybody's game. When all the psychotics and psychoneurotics and neurological patients are lumped together, they constitute many more than half of the sick in this country. A look at Veterans Administration statistics will bear this out. If you are looking for new land to break to the plow, here it is, stretching beyond the horizon. Our changing economic structure is making you into the logical plowman in place of the universities. I commend these rich unbroken fields to you. Their potential harvests are tremendous.

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